Three-Dimensional Echocardiography in Mitral Valve Disease

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THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN MITRAL VALVE DISEASE

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CONTENTS

CHAPTER 1

THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN MITRAL VALVE DISEASE **3**
Eur J Echocardiogr 2005;6:443-54

CHAPTER 2

NEW QUANTITATIVE THREE-DIMENSIONAL ECHOCARDIOGRAPHIC INDICES OF MITRAL VALVE STENOSIS. **20**
Submitted

CHAPTER 3

ADDITIONAL VALUE OF THREE-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY FOR PATIENTS WITH MITRAL VALVE STENOSIS UNDERGOING BALLOON VALVULOPLASTY **31**
J Am Soc Echocardiogr 2003;16:841-9

CHAPTER 4

QUANTITATIVE ASSESSMENT OF MECHANICAL PROSTHETIC VALVE AREA BY 3-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY **48**
J Am Soc Echocardiogr 2001;14:723-31

CHAPTER 5

ANTERIOR MITRAL VALVE ANEURYSM: EVALUATION BY THREE-DIMENSIONAL ECHOCARDIOGRAPHY **63**
J Am Soc Echocardiogr 1998;11:673-6

CHAPTER 6

ASSESSMENT OF THE LEFT ATRIAL APPENDAGE MECHANICAL FUNCTION BY THREE-DIMENSIONAL ECHOCARDIOGRAPHY **68**
Eur J Echocardiogr 2002;3:207-13

CHAPTER 7 **79**

SUMMARY **79**

Chapter 1

THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN MITRAL VALVE DISEASE

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Eur J Echocardiogr 2005;6:443-54

INTRODUCTION

Echocardiography has evolved into the most predominant diagnostic imaging technique in Cardiology. Over the last 5 decades the diagnostic capability of echocardiography has increased dramatically from M-mode to two-dimensional (2D) imaging. Recent advances in ultrasound instrumentation and computer technology have led to three-dimensional (3D) echocardiography, thus introducing a new era in cardiovascular imaging.[1]

Every imaging technique in Cardiology aims at a complete visualization and comprehensive assessment of cardiac morphology and pathology as the heart is a complex geometric structure. Therefore, analysis of the heart in motion in all three or four (including time) dimensions can further facilitate and enhance the diagnostic capabilities of echocardiography. 3D echocardiography is still in its evolution and at the phase of early adaptation with respect to its clinical application. It should complement current echocardiographic techniques by providing better understanding of the topographical aspects of pathology and refined definition of the spatial relationships of (intra)cardiac structures. Furthermore, it provides new indices not described by 2D echocardiography and makes more accurate the existing ones.[2]

The assessment of patients with mitral valve disease is one of the most challenging and promising clinical applications of 3D echocardiography. We discuss the 3D anatomy of the mitral valve as well as the feasibility, accuracy and incremental value of 3D echocardiography in the evaluation of mitral valve disease.

3D RECONSTRUCTION

There are two main approaches of 3D reconstruction. The first is random or freehand scanning which is based on free motion of the ultrasound transducer. Its position in space is located by an acoustic, electromagnetic or mechanical arm location device. The transthoracic approach is used in this mode of acquisition. The limitation of this method is that accurate endocardial border identification is restricted because of big gaps between imaging planes. The second approach is sequential scanning where the ultrasound motion is predetermined in linear, fan-like or rotational ways. Tranthoracic or transesophageal approach is used for this mode of data acquisition. Both the sequentially or randomly collected 2D images are off-line processed by the computer using interpolation algorithms so that the gaps between individual images are filled and finally a volumetric 3D data set is generated. There are several ways to present the data in the 3D volumetric data set. The most used are:

Anyplane echocardiography. This mode of presentation allows the examiner to generate 2D tomographic images in any desired orientation which can be physically unobtainable by conventional 2D echocardiography.

Volumetric rendering technique. This 3D reconstruction creates images resembling the true anatomy of the heart. By choosing a cutting plane and reconstructing the image beyond this plane the heart can be opened as if it was done by a surgeon. Different structures can be examined en face with better perception of the anatomic relationships.

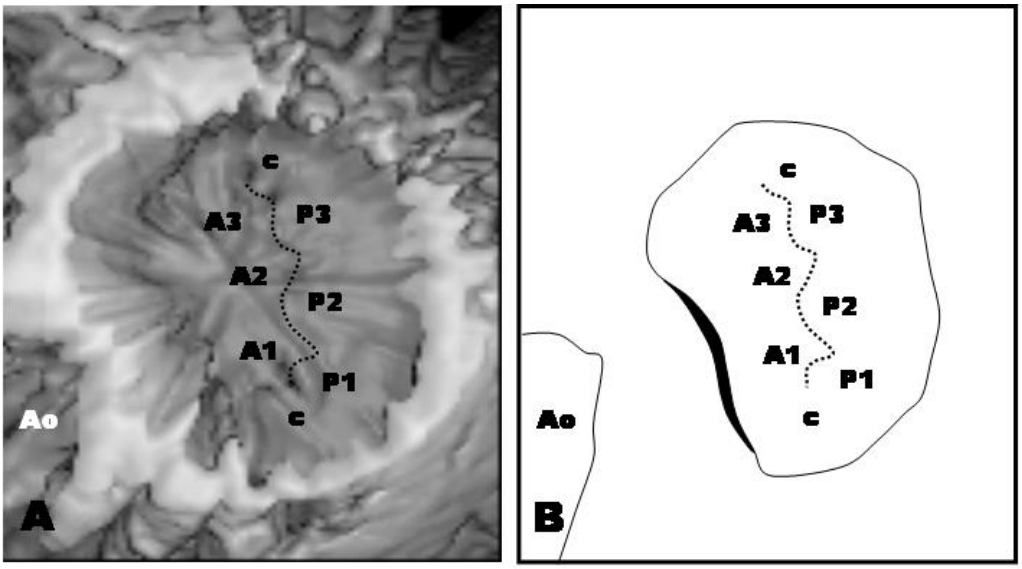

Figure 1 *A normal mitral valve during systole viewed from the left atrium (**A**). (**B**) Schematic diagram depicting the segments/scallops of the anterior leaflet: **A1** – anterolateral, **A2** – middle, **A3** – posteromedial, and posterior leaflet: **P1** – anterolateral, **P2** – middle, **P3** – posteromedial, **c** – commissures.*

The ideal for 3D reconstruction is **real-time 3D echocardiography** (RT3D). The system uses a novel matrix phased-array transducer with parallel processing to scan a pyramidal volume. In a pyramidal volume, the images are displayed as anyplane or volume rendered images immediately. Second generation matrix transducer became recently available for clinical studies.

Further advances in computer technology have enabled encoding of color flow Doppler data together with gray-scale imaging and 3D presentation of Doppler flow events with surrounding cardiac anatomy.[3]

FUNCTIONAL ANATOMY OF THE MITRAL VALVE

3D topography of the mitral valve

3D echocardiography by viewing the mitral valve from the left atrium shows that the anterior and posterior mitral leaflets have several indentations dividing them into segments or scallops (Figure 1). The anterior leaflet has three segments: A1 – anterolateral, A2 – middle, A3 – posteromedial. Similarly, the posterior leaflet has three segments: P1 – anterolateral, P2 – middle, P3 – posteromedial. The anterior and posterior leaflets are fused for 3 to 8 mm medially and laterally at the trigones and usually form distinct commissures (anterolateral and posteromedial). The anterior leaflet comprises roughly two thirds of the valve area, is about twofold longer than the posterior leaflet, and is somewhat triangular. The posterior leaflet is more elongated and rectangular. The anterior leaflet is attached to the septum and fibrous annulus of the heart, and it is relatively nondistensible. Although the anterior leaflet accounts for two thirds of the mitral valve area, its attachment to the mitral annulus accounts for only approximately one third of the mitral annular circumference. The anterior mitral leaflet spans the distance between the two fibrous trigones and is in direct continuity with the

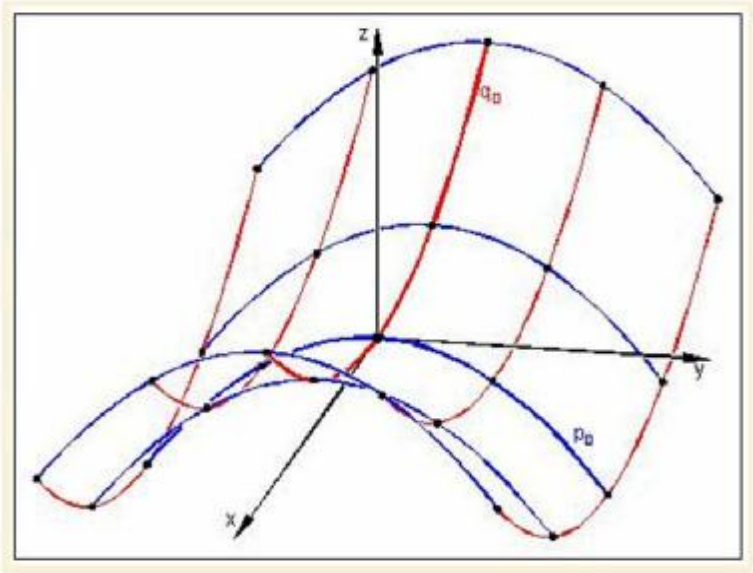

Figure 2 *Hyperbolic paraboloid.*

noncoronary aortic valve leaflet. The posterior mitral valve leaflet is attached to the posterior two thirds of the mitral annulus, which runs along the free wall of the left ventricle and is primarily muscular with little fibrous tissue (explaining its tendency to distend and elongate).

Nonplanarity of the mitral valve and annulus

Based on the studies conducted in an effort to refine the diagnosis of mitral valve prolapse, the geometric shape of the mitral valve and its annulus was defined. It has been documented that the mitral annulus and leaflets are nonplanar saddle-shaped structures which are equivalent with the so called hyperbolic paraboloid, a geometric surface of which all sections parallel to one coordinate plane are hyperbolas and all sections parallel to another coordinate plane are parabolas (Figure 2). There are two high points (peaks) lying anteriorly and posteriorly at the aortic insertion and posterior left ventricular wall and two low points (troughs) closest to the apex located medially and laterally (Figure 3). According to Levine et al. the maximum deviation from planarity, i.e., the distance between the highest and lowest points of the mitral annulus, is on average 1.4 $\pm$ 0.3 cm.[4] Regarding the leaflet-annular relations, in mediolateral view (four-chamber view in 2D echocardiography) the leaflets can appear above the mitral annulus but in anterolateral view (parasternal long-axis view in 2D echocardiography) they do not ascend the annulus. That is the reason why in the four-chamber view in the era of 2D echocardiography superior leaflet displacement was wrongly diagnosed as prolapse in otherwise normal individuals. The leaflet-annular nonplanarity is rational in two ways. First, as the base of the left ventricle decreases in circumference during systole but the leaflets do not contract, the mitral annular area can decrease in some way of folding which is achieved by lowering of the distance between high and lower points of the annulus.[5,6] Second, the saddle-shape provide a configuration capable of withstanding the stresses imposed by left ventricular pressure in systole. Salgo et al. studied the effect of nonplanarity on stress reduction.[7] Two shape factors which have synergistic effect on

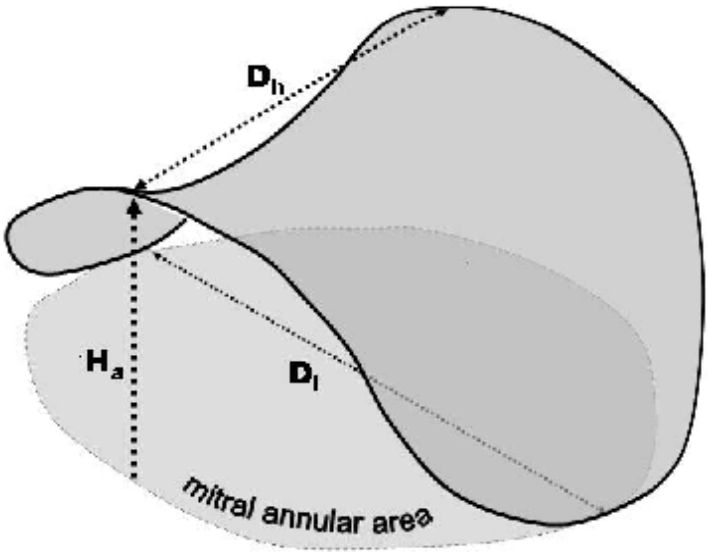

Figure 3 *Schematic presentation of the nonplanar, saddle-shaped mitral valve and its characteristic parameters:* D_h *- distance between high points;* D_l *- distance between low points of the annulus;* H_a *- annular height. The mitral annular area is measured as an area of the least squares plane.*

stress reduction have been identified: leaflet billowing and annular nonplanarity. The saddle-shape of the mitral annulus was preserved across 3 mammalian species (human, sheep and baboons) with an annular height commissural width ratio of about 15%. Their data suggest that the nature conserves the saddle-shaped configuration of the annulus for a mechanical benefit.

Dynamics of the mitral annulus

There are two studies by Flachskampf et al. and Kaplan et al. which provide insights into the dynamics of the mitral annulus.[5,6] According to these studies the mitral annular area was on average 5-6 cm^2/m^2 corrected for body surface area (because of nonplanarity an area projected into the least squares plane was measured). This area decreased in systole for about 24%. The mechanism by which it was achieved was elipticalization due to reduced distance between two high points with increase in annular height and eccentricity and smaller amount by reduced distance between two low points (Figure 4). At the same time the basic features of nonplanarity (2 high and 2 low points) were preserved throughout the cardiac cylce.

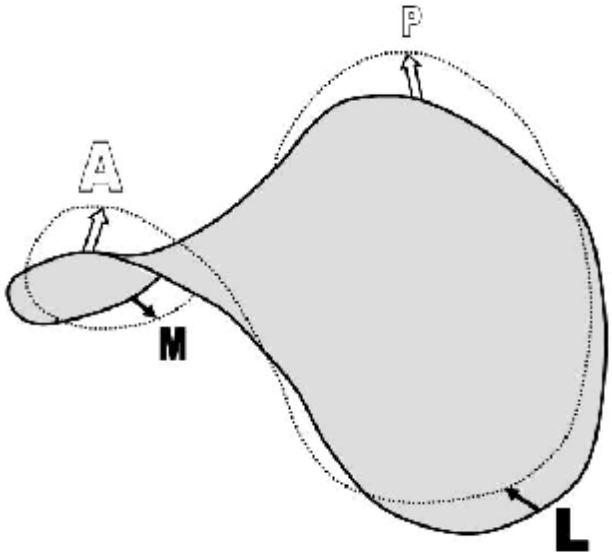

Figure 4 *Schematic presentation of the dynamics of the mitral annulus. The mechanism is achieved by reducing the distance between anterior (**A**) and posterior (**P**) high points with increase in annular height and reducing the distance between medial (**M**) and lateral (**L**) low points of the mitral annulus.*

MITRAL STENOSIS

The severity of mitral stenosis is assessed mainly by estimation of the mitral valve area.[8] Currently, the available 2D echocardiographic and Doppler techniques have their well-known limitations. The advent of 3D echocardiography has refined the assessment of mitral valve area to such an extent that today it is considered as a gold standard. Besides, 3D echocardiography has introduced new indices which further improve the diagnosis of mitral stenosis. By means of 3D echocardiography it is possible to assess the morphology of the mitral valve also in balloon mitral valvuloplasty what is important in the evaluation of the mechanism and success of the procedure.

Assessment of mitral valve area

In a 3D homogeneous data set using anyplane echocardiography it is possible to pinpoint the cut plane to the tips of the mitral valve so the true anatomic valve area can be measured (Figure 5). The advantage of this method is, contrary to 2D echocardiography, that proper alignment of the cut plane is controlled in a 3D data set. It is important because errors due to malpositioning can be obviated. It has been shown that malpositioning errors can achieve up to 88% (1.5 cm^2) in the measurement of the mitral valve area what is not acceptable in the management of patient with mitral stenosis.[9] In addition, assessment of the anatomic mitral valve area is advantageous because it is hemodynamically independent contrary to effective mitral valve area (measured by pressure half-time and PISA methods) which is hemodynamically influenced by associated abnormalities (aortic insufficiency, increased left ventricular stiffness).

In the first studies carried out by Kupferwasser et al. and Chen et al. the mitral valve area was assessed by anyplane 3D transesophageal echocardiography (TEE).[10,11]

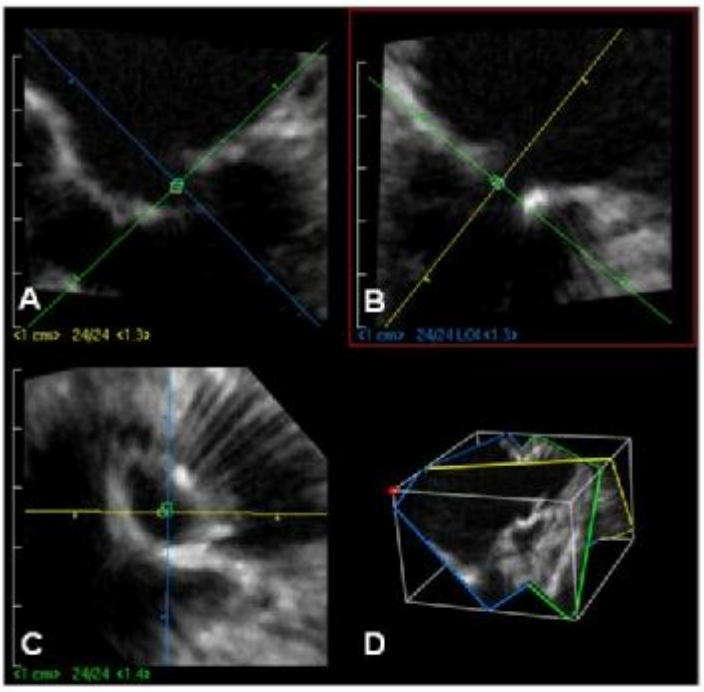

Figure 5 *Mitral valve area measurement using anyplane echocardiography. Two long-axis cut planes perpendicular to each other (**A** and **B**). By guidance of line of intersection, optimal short-axis cut plane was selected (**C**). 3D data set and spatial alignment of 3D cut planes (**D**).*

The mitral valve area assessed by 3D echocardiography was compared with the mitral valve area measured by 2D methods (2D planimetry and pressure half-time) and invasively assessed mitral valve area according to the Gorlin formula. Only Kasliwal et al. compared the mitral valve areas by 3D echocardiography with the true mitral orifice measured directly at operation.[12] The comparison achieved a high degree of agreement (r=0.95) thus 3D echocardiography, today, can be considered as a new clinical standard in the assessment of the anatomic mitral valve area. 3D echocardiography has been shown to be accurate in the assessment of mitral valve area also in the transthoracic approach. Sugeng et al. confirmed that freehand 3D transthoracic echocardiography comparing with 2D planimetry, pressure half-time and the PISA methods is the most accurate when it was compared with invasively determined mitral valve area according to the Gorlin formula.[13] The most attractive is definitely RT3D echocardiography which allows on-line assessment of the mitral valve area. Images are displayed as two simultaneous intersecting orthogonal long-axis scans (B-mode scans) and two perpendicular short-axis scans (C-mode scans). These C-mode scans allow the display of short-axis views of the mitral valve from an apical transducer position. Binder et al. found out that RT3D echocardiography comparing with 2D planimetry and pressure half-time methods allows accurate measurement of the mitral valve area from the transthoracic approach.[9] It is of course evident in patients with an adequate acoustic window.

New indices of mitral stenosis

Thickening of mitral leaflets in rheumatic mitral stenosis is a well-known phenomenon. Limbu et al. were the first who quantified the mitral valve volume in vivo in normal subjects and patients with rheumatic mitral stenosis (Figure 6).[14] The mitral

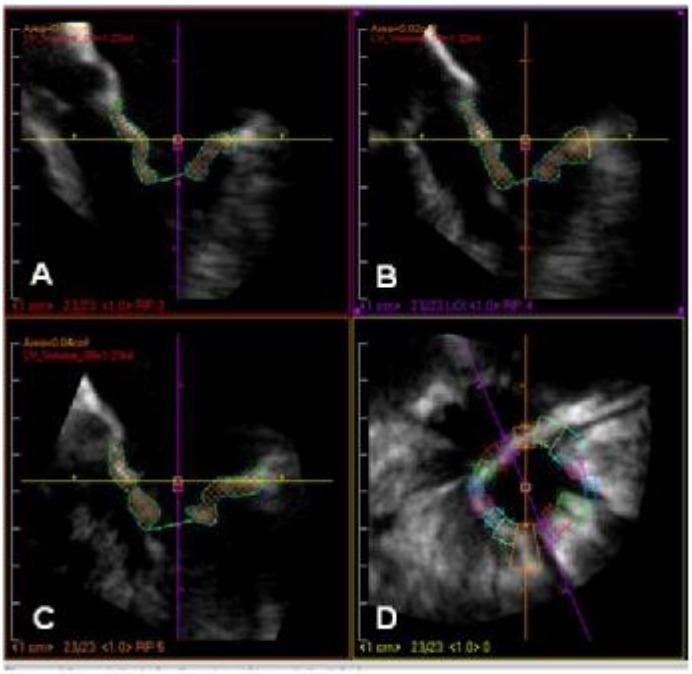

Figure 6 *Volume measurement of mitral leaflets by anyplane echocardiography. Three long-axis cut planes constructed around center axis of mitral apparatus (**A**, **B**, and **C**). In these views boundaries of mitral valve subvolumes were traced and their corresponding short-axis views are presented in short-axis cut plane (**D**). In all, 8 slices were used for volume computation.*

valve volume in normal individuals was on average 4.5 ml and in patients with mitral stenosis 9 ml. When they divided patients with mitral stenosis into the sinus rhythm and atrial fibrillation groups, patients with atrial fibrillation had a propensity to have a larger mitral valve volume and were older than patients with sinus rhythm. Thus, etiologic relationship between atrial fibrillation and further enlargement of the mitral valve volume was speculated. Gilon et al. studied in vitro the hypothesis that the stenotic mitral valve influences the pressures and flows not only by cross-sectional area but also by 3D geometry of the stenotic valve proximal to the orifice.[15] With the use of 3D echocardiography and stereolitography they constructed by laser polymerization different shapes of mitral valve: domed, intermediate and flattened. Coefficient of contraction was calculated as effective area divided by anatomic orifice area. Coefficient of contraction decreased as the mitral valve was flattened. The study confirmed, that variations in contraction coefficient (i.e., the 3D geometry of the mitral valve) led to varying pressure gradients that were up to 40% higher for the flattest valves. Thus, doming valves permit a higher cardiac output than flat ones.

3D echocardiography in balloon mitral valvuloplasty

3D echocardiography by volume rendering allows visualization of the mitral valve en face either from the left atrium or the left ventricle. Applebaum et al. evaluated the mechanism of balloon valvuloplasty by 3D echocardiography.[16] Volume rendered 3D images enabled visualization of commissural splitting and leaflet tears not seen on 2D (Figure 7, 8). They found that balloon mitral valvuloplasty was more successful when complete splitting was achieved as compared with partial splitting. Moreover, in 38% of patients in whom an increase of mitral regurgitation developed, tear was visualized by

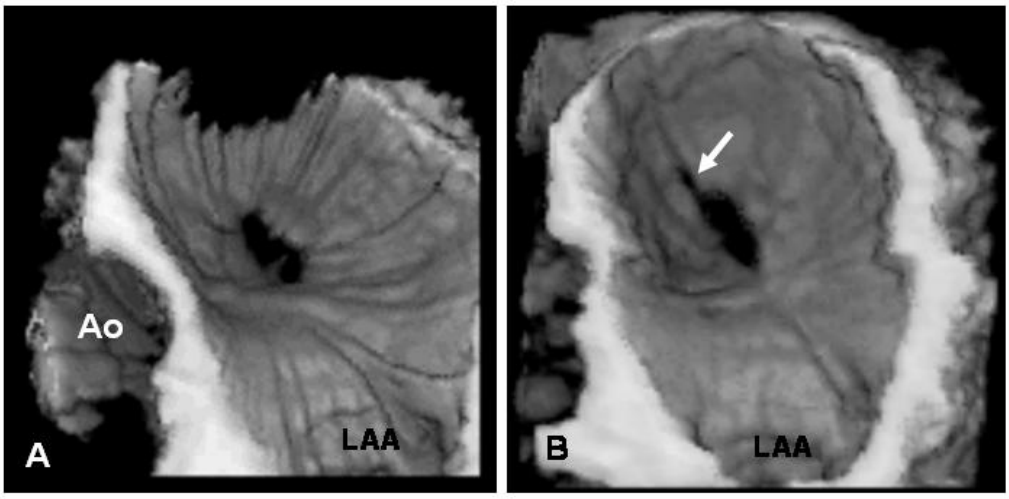

Figure 7 *Diastolic frames of the 3D reconstruction of the mitral valve orifice as seen from the left atrium before* ***(A)*** *and after* ***(B)*** *balloon valvuloplasty. A posteromedial commissural split is visualized* ***(arrow)****.* ***Ao*** *– aorta;* ***LAA*** *– left atrial appendage.*[17]

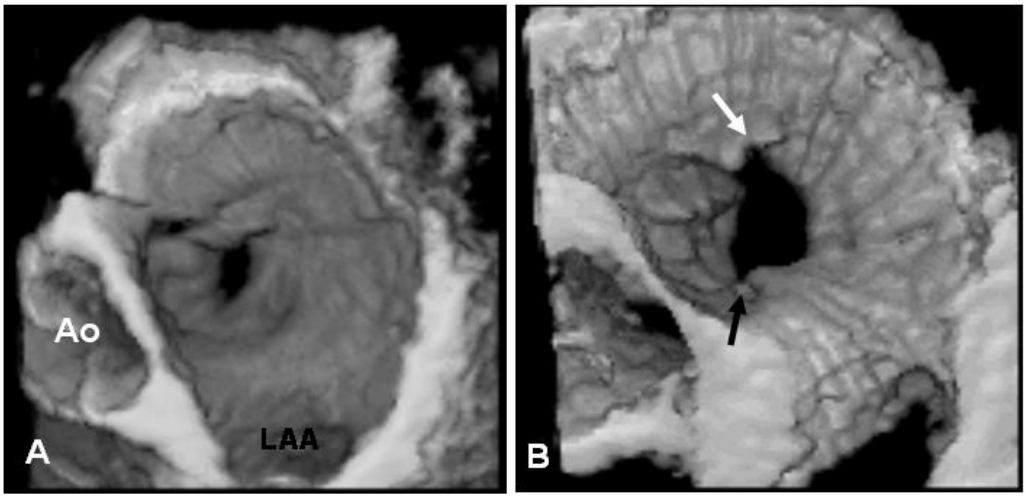

Figure 8 *Diastolic frames of the 3D reconstruction of the mitral valve orifice as seen from the left atrium before* ***(A)*** *and after* ***(B)*** *balloon valvuloplasty. A posteromedial* ***(white arrow)*** *and anterolateral* ***(black arrow)*** *commissural split is visualized.* ***Ao*** *– aorta;* ***LAA*** *– left atrial appendage.*[17]

3D. Our group, Langerveld et al., conducted a similar study where 3D TEE enabled a better description of the mitral valvular anatomy following balloon mitral valvuloplasty, comparing to 2D echocardiography. In addition, significant relation of mitral valve volume before valvuloplasty to a successful procedure was found.[17]

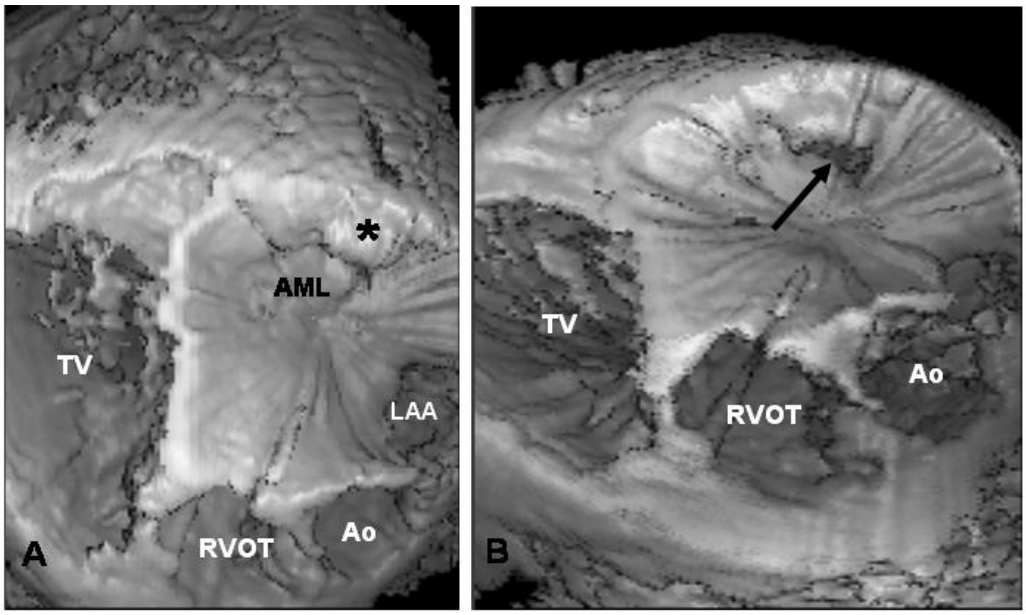

Figure 9 (A) *View of the mitral valve prolapse as seen from the left atrium. The middle segment (*) protrudes into the left atrium.* ***(B)*** *When the whole data set is turned a crack due to noncoaptation is visualized* ***(arrow)****.* ***AML*** *– anterior mitral leaflet;* ***TV*** *– tricuspid valve;* ***RVOT*** *– right ventricular outflow tract;* ***Ao*** *– aorta;* ***LAA*** *– left atrial appendage.*

MITRAL VALVE PROLAPSE

Echocardiography is the most utilized imaging modality for diagnosis of mitral valve prolapse. M-mode and 2D echocardiography frequently lead to both false-positive and false-negative diagnoses. It is because of the nonplanar leaflet-annular relations of the mitral valve. Prolapse is generally defined as a displacement of a bodily part from its normal position or relations. By 3D echocardiography it is possible to visualize the mitral valve en face from either the left atrium or the left ventricle.[18,19] In volume rendered images looking down in the left atrium, mitral valve prolapse is viewed as a convexity or bulge, and often as bright area when compared with the rest of the mitral leaflet. Looking up in the left ventricle mitral valve prolapse appears as a spoon-like depression. In patients with mitral valve prolapse and mitral regurgitation a crack due to noncoaptation can be identified (Figure 9). 3D echocardiography allows accurate identification and quantification of prolapse of individual scallops/segments of the mitral valve leaflets (Figure 10). Two intraoperative studies, conducted by Ahmed et. al and Chauvel et al. confirmed that topography of prolapsing scallops/segments by 3D echocardiography was correct in 78% and 86%, respectively. Contrary to 2D echocardiography, 3D echocardiography allowed measurements of the area and width of the prolapsed portion of the leaflet as well as mesurements of the circumference of the posterior part of the mitral annulus. This information could aid the surgeon in deciding the extent of valvular tissue resection.[20,21]

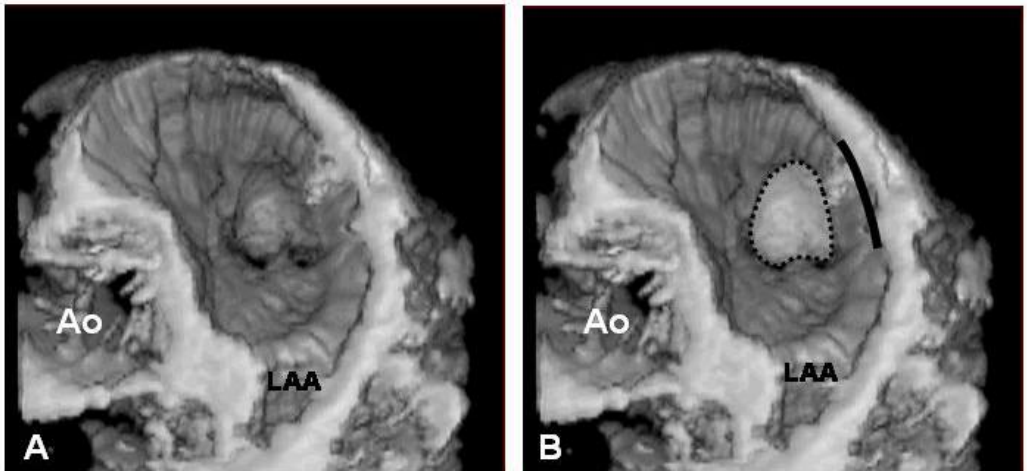

Figure 10 *(**A**) Prolapse of the middle segment of the posterior mitral leaflet viewed in systole from the left atrium. (**B**) Measurement of the area and width of the prolapsing segment.* ***Ao*** *– aorta;* ***LAA*** *– left atrial appendage.*

MITRAL REGURGITATION

Accurate evaluation of mitral regurgitation severity is a challenging task in clinical cardiology. The current 2D echocardiographic methods used to quantify mitral regurgitation have their well-known limitations. 3D echocardiography has the potential to improve the assessment of mitral regurgitation by facilitating the visualization of complex mitral anatomy in three dimensions and providing more accurate quantification of regurgitant color Doppler flow events.[22-24] Investigators have aimed to validate 3D echocardiography mainly in the measurements of regurgitant jet volumes, flow convergence surface area and anatomic regurgitant orifice area .

3D quantification of regurgitant jet volume

The first studies used volume rendered gray-scale imaging to visualize Doppler flow in three dimensions.[25,26] The differentiation of regurgitant jets from surrounding cardiac structures was difficult. The volume of the mitral regurgitant jet was measured by „summation of discs“ method.[27] Later, De Simone and colleagues proposed a method of color coding of regurgitant mitral jets derived from digital data.[28-32] Jet volumes were calculated by segmentation with automatic selection of turbulence and high-velocity components or volume units (voxels) containing the selected Doppler data. This mode of 3D color flow imaging recognized different patterns of eccentric regurgitant jets, not described previously, such as cylinder, tongue, spiral and spoon-like patterns. What is more important, calculation of the jet volume was capable to accurately quantify asymmetrical jets. Recently, Sugeng et al. improved the method of color encoding of regurgitant jets together with gray-scale imaging of the surrounding cardiac anatomy.[33] This improved technique provided information on the origin and extent of the dehiscence in case of paravalvular leaks, as well as insight into the direction of the regurgitant jets.

Flow convergence zone and 3D echocardiography

The flow convergence or proximal isovelocity surface area (PISA) method is based on the phenomenon that flow accelerates towards the regurgitant orifice and forms

a series of concentric hemispheric shells of increasing velocity. According to the continuity concept, the flow rate is calculated by multiplying the isovelocity surface area and its corresponding aliasing velocity. Thus, accurate measurement of the flow convergence surface area is the most important aspect for obtaining accurate flow rate. Conventional 2D methods rely on assumptions that the isovelocity surface is hemispheric or hemielliptic. However, 3D imaging has revealed that the morphology of the flow convergence region is more complex and unpredictable in shape.[34] Since 3D can display the entire flow convergence region en face viewing from the left atrium, a more accurate assessment of its area can be done without the need to make geometric assumptions. Three-dimensional flow convergence based methods have been shown to accurately predict the flow rate.[35,36]

Regurgitant orifice area measurement by 3D echocardiography

The regurgitant orifice area is a measure of valvular incompetence useful for assessment of mitral regurgitation. Up to now, measurement of the regurgitant orifice area was based on Doppler methods which calculated the effective orifice area. 3D echocardiography provides an opportunity to visualize the regurgitant orifice and so anatomic regurgitant orifice area measurement. It has been shown that anatomic regurgitant orifice area measured directly by planimetry from 3D volume rendered images correlates well with effective regurgitant orifice area calculated by the proximal convergence method.[37-39]

FUNCTIONAL MITRAL REGURGITATION

Functional mitral regurgitation is defined as an insufficiency of the structurally normal mitral valve developing as a consequence of regional or global left ventricular dysfunction. It is a complication of either chronic ischemic heart disease, dilated or hypertrophic cardiomyopathy. Functional mitral regurgitation is associated with increased mortality independent of left ventricular dysfunction. The mechanisms which participate on the development of functional mitral regurgitation are related to the geometry of the mitral valve, mitral annulus and papillary muscles. Since the relation of these anatomical structures is explicitly three dimensional, 3D echocardiography provides the best mode to study their relationship.

Mitral annular geometry

Flachskampf et al. and Kaplan et al. have shown by 3D echocardiography that functional mitral regurgitation is associated with annular dilation and its reduced cyclic variation.[5,6] Compared with normal subjects, the annulus in patients with functional mitral regurgitation is larger and has greater mitral annular area, longer perimeter, reduced annular height and eccentricity, and increased distance between high points of the mitral annulus.

Leaflet geometry

Using RT3D echocardiography, Kwan et al. studied the difference of mitral valve deformation between ischemic and dilated cardiomyopathy with significant functional mitral regurgitation.[40] Mitral valve tethering has been found as a strongest determinant of mitral regurgitation severity and the pattern of mitral valve deformation was asymmetrical in ischemic heart disease, whereas it was symmetrical in dilated cardiomyopathy.

Papillary muscles geometry

Several studies have been performed in an effort to elucidate a 3D papillary muscle-mitral relation.[41-44] The results of these studies show that especially medial and posterior shift of the ischemic medial papillary muscle, measured by 3D reconstruction, is related to the development of functional mitral regurgitation.

MITRAL VALVE REPAIR AND 3D ECHOCARDIOGRAPHY

Mitral valve repair has become more common in the last decade making up more than half of the mitral valve procedures.[45] Various techniques have been proposed for valve reconstructions.[46-48] The decision „how to operate“ depends on the underlying pathology of the mitral valve diagnosed by preoperative echocardiography. Conventional 2D echocardiography is a useful guide for accurate surgical analysis, however, in complex valvular pathologies some spatial relations and different structural features can be perceived erroneously even by experienced echocardiographer. Therefore, the technique of repair is frequently modified in the operating room by close examination of the mitral valve, but the surgeon is challenged by limited time, operating field and nonphysiologic condition of the heart being devoid of blood. 3D echocardiography has the potential to overcome these difficulties by showing the heart in „surgeon's view“ even in more physiologic state as during operation.

There are few published data regarding the feasibility of 3D echocardiography in the operation theater. Abraham et al. demonstrated that 3D echocardiography can detect new morphologic findings (mainly valve fenestrations) in 25% of cases, not seen on 2D TEE. In 1 patient 3D TEE resulted in a decision to perform valve repair instead of replacement. As it mentioned previously, 3D TEE has been proved to be accurate in identifying the location of the prolapsing segment and quantifying the amount of the prolapsed tissue by measuring the area or the width. This information could aid the surgeon in deciding the extent of mitral valve resection.[49]

CONCLUSION

3D echocardiography allows visualization of the heart in a way different from 2D echocardiography, as it looks in a true reality. The assessment of the morphology, function and pathology of the heart, and especially the mitral valve apparatus by 3D echocardiography becomes more accurate. Comparing with 2D echocardiography, 3D echocardiography offers advantages for the morphologic and quantitative assessment of mitral valve stenosis, prolapse and regurgitation. It appears that 3D echocardiography has the potential for planning operations and assessing interventional or surgical results. Furthermore, 3D echocardiography provides new quantative indices unobtainable by conventional 2D imaging. Both technical improvement and larger studies will enhance the clinical applicability of 3D echocardiography in the nearest future.

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Chapter 2

NEW QUANTITATIVE THREE-DIMENSIONAL ECHOCARDIOGRAPHIC INDICES OF MITRAL VALVE STENOSIS.

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Submitted

ABSTRACT

Aims

We studied the value of quantitative three-dimensional echocardiography (3DE) in the evaluation of mitral valve stenosis using the measurement of the mitral valve area (MVA) with two new indices: the doming volume and mitral valve volume.

Methods and results

A total of 45 consecutive patients with mitral valve stenosis, 36 patients (80%) with sinus rhythm and 9 patients (20%) with atrial fibrillation, were studied. In 27 patients (60%), concomitant mitral regurgitation and in 18 patients (40%), concomitant aortic regurgitation was present. MVA was measured using Doppler with the pressure half-time (PHT) method. Following a diagnostic multiplane TEE procedure for clinical evaluation, data for 3DE were acquired with a rotational acquisition mode. MVA was assessed by anyplane echocardiography (APE) and from surface rendered images. Moreover, the doming volume, i.e., the volume subtended by the anterior and posterior mitral valve and annular cut plane was measured by APE using an average rotation method with 10 slices. Comparing PHT-derived with 3DE-derived MVA's, using both APE and surface rendered images, only moderate correlations were observed: PHT-derived MVA versus APE-derived MVA: $r=0.74$, $p<0.0001$; PHT-derived area versus 3DE-surface rendered MVA: $r=0.70$, $p<0.0001$. Multiple linear regression analysis showed a relation of atrial fibrillation to the doming volume ($p=0.04$), but not to PHT-derived MVA ($p=0.28$), APE-derived area ($p=0.33$) and mitral valve volume ($p=0.08$). Associated valvular regurgitation had no effect on the MVA's measured by Doppler PHT and both 3DE methods. Comparison of patients with MVA $< 1cm^2$ and MVA $> 1\ cm^2$ revealed significant difference in mitral valve volume: mean mitral valve volume in critical stenosis was 3.7 ml versus 1.4 ml in non-critical stenosis ($p=0.04$).

Conclusions

Only moderate correlations between 3DE and Doppler-derived MVA's were observed. Measurement of the doming volume allows quantification of the 3DE geometry of the mitral apparatus. Patients with conical or funnel-like geometry are more likely to have sinus rhythm, whereas, patients with flat geometry are likely to have atrial fibrillation. Mitral valve volume can be used for the evaluation of mitral stenosis severity. These new 3DE indices might be used for selection of patients for balloon valvuloplasty.

Key words: Mitral valve stenosis, three-dimensional echocardiography, transesophageal echocardiography.

INTRODUCTION

Analysis of the heart with three-dimensional echocardiography (3DE) facilitates and enhances the diagnostic capability of echocardiography.[1] 3DE complements the current echocardiographic techniques by providing: 1) new images on anatomy and pathology of the heart, 2) more accurate quantitative data in comparison to two-dimensional echocardiography (2DE), and 3) new quantitative information and novel indices.

In this study, we evaluated the value of quantitative 3DE in the evaluation and grading of mitral valve stenosis, using 3DE measurements of the mitral valve area (MVA), as well as two new indices: the mitral valve doming volume and the mitral valve volume.

PATIENTS AND METHODS

We studied a consecutive cohort of 45 patients (7 men and 38 women) with mitral valve stenosis referred to the Department of Cardiology between June 1996 and July 2000. Mean age was 50.3 years (range from 18 to 74 years). The diagnosis of mitral valve stenosis was made by transthoracic 2DE and subsequent multiplane transesophageal echocardiography (TEE). During the examination, 36 patients (80%) had sinus rhythm and 9 patients (20%) atrial fibrillation. In 27 patients (60%), concomitant mitral regurgitation was present (17 patients with grade 1+, 8 patients grade 2+, and 2 patients grade 3+). In 18 patients (40%), aortic insufficiency was present (16 patients grade 1+, 1 patient grade 2+, and 1 patient grade 3+). The grade of regurgitation was assessed by color flow mapping described elsewhere.[2,3]

Two-dimensional echocardiography

The examination was performed using a Hewlett-Packard Sonos 2500 or 5500 system (Hewlett-Packard Co., Andover, Mass., USA) with a transthoracic 2.5 or 3.75 MHz probe and a 5MHz, 64-element multiplane TEE. Mitral valve area was assessed by the Doppler pressure half-time (PHT) method as described by Hatle et al.[4]

Three-dimensional echocardiography

Following a diagnostic TEE procedure for clinical evaluation, the probe was located at mid-esophageal level. A test sequence with 180° rotation of the transducer array was done to ascertain that the mitral valve was encompassed within the conical acquisistion volume. Cross-sectional cardiac images were obtained at 3° increments starting from the horizontal plane. EKG and respiratory gating were performed for optimal spatial and temporal registration. The cross-sections were stored on a magneto-optical disk. Image processing and finally dynamic 3DE reconstruction were performed off-line with the Echo-scan developed by TomTec GmbH (Munich, Germany). Processing and image reconstruction required on average 5 minutes. All 45 scans were suitable for 3DE reconstruction.

After postprocessing, a conical data set was reconstructed on which anyplane echocardiography (APE) and surface rendered images could be obtained. Two long-axis views through the mitral valve, nearly perpendicular to each other, were defined by navigation of the lines of intersection. Short-axis cut planes were further positioned at the mitral valve cusp tips, which was selected for area measurement by planimetry (Figure 1). It was the smallest anatomic area of the mitral valve. In the same manner surface rendering was performed. Gain threshold was set to the level optimal for spatial

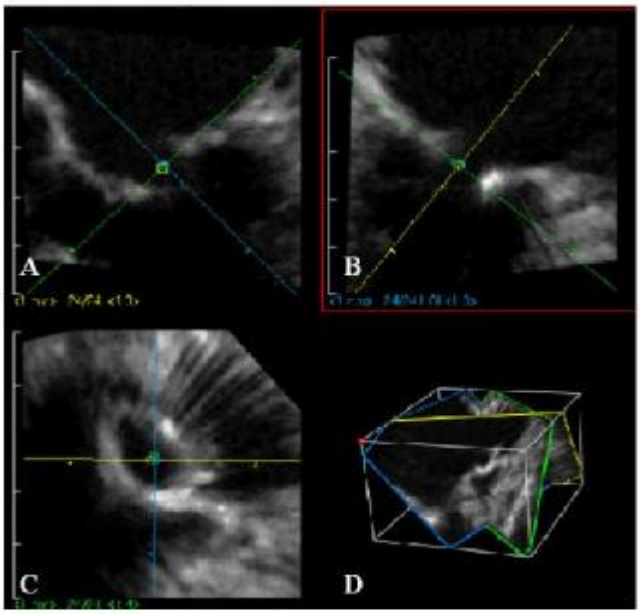

Figure 1 *MVA measurement by APE. The two cut planes in the long axis of the mitral valve A and B were generated in a 3DE data set (D). Short axis cut plane, which cuts the mitral valve just at the cusp tips, was defined by navigation of the lines of intersection (C).*

perception of the structures. Multiple dynamic short-axis 3DE images with different angulations were reconstructed from the data set and the image with a cut plane closest to being parallel with the plane of the mitral valve orifice was selected for three-dimensional surface area measurement by planimetry (Figure 2).

For purpose of quantification of the doming volume we also measured the volume subtended by the mitral valve and annular cut plane. The TomTec EchoView system was used for both doming volume and mitral valve volume calculations. The average rotation method with 10 slices was used. In each of them, the area subtended by the anterior and posterior mitral valve as well as annular cut plane was traced. The volume of each slice was summed up and finally the doming volume was calculated (Figure 3). The boundary tracing method was also used for volume computation of the mitral valve leaflets, as described by Limbu et al.[5] Average rotation method with 8 slices was selected. The centre axis of the mitral apparatus around which the slices were constructed, was selected by quidance of the line of intersection display. The boundaries were traced by the mouse-driven cursor. After the volume of each slice had been calculated, the system summed the corresponding subvolumes and finally calculated the volume of the entire mitral valve (Figure 4).

For the evaluation of intra- and interobserver variability, the measurements of the mitral valve doming volume and mitral valve volume were repeated approximately l month apart in 10 randomly selected patients by the same (GV) and another observer (HM), respectively.

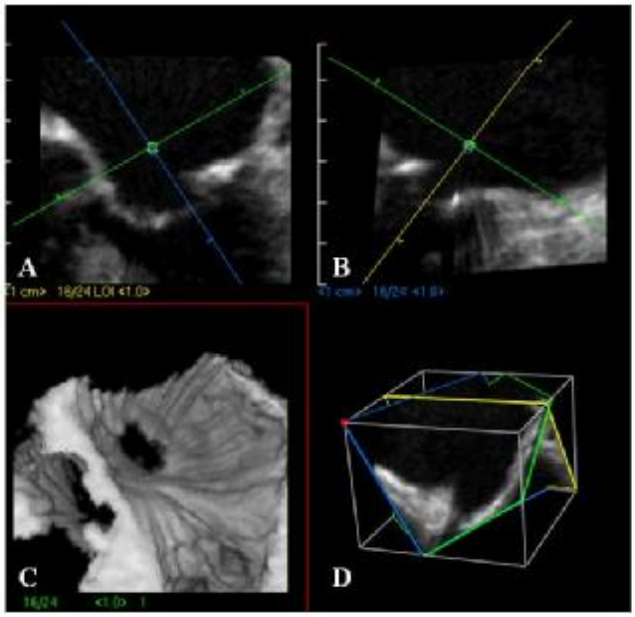

Figure 2 *MVA measurement obtained from 3DE surface rendered image. In two long axis views through the mitral valve (A and B), 3DE surface rendered image was reconstructed so that the viewing cut plane was parallel with the plane of the mitral valve orifice (C). D represents a homogeneous 3DE data set.*

Statistical analysis

Data are expressed as mean ± standard deviation. Significant differences between groups were demonstrated using paired t test. Differences were considered statistically significant at a p-value of <0.05. Linear regression analysis was used to determine the correlation between 3DE and PHT-derived areas. Analysis of agreement was performed using the method proposed by Bland and Altman.[6] Limits of agreement were defined as mean ± 0.96 x SD of differences. Multiple linear regression analysis was used for the assessment of relation between different data. Observer variability was expressed in coefficients of variation calculated as standard deviation of differences between measurements divided by the mean value.

RESULTS

Mitral valve area

Mitral valve area measured by the Doppler PHT method ranged from 0.7 to 2.7 $cm,^2$ mean 1.42 ± 0.55 $cm.^2$ Data obtained by 3DE were as follows: MVA by APE 1.31 ± 0.54 cm^2 (range from 0.5 to 2.6 cm^2), valve area from surface rendered images 1.23 ± 0.53 cm^2 (range from 0.4 to 2.4 cm^2). Comparing PHT-derived MVA's with 3DE-derived areas by both APE and surface rendering, we found moderate correlations: PHT versus APE-derived area: r=0.74, p<0.0001, y=0.77x + 0.40; PHT-derived area versus 3DE surface area r=0.70, p<0.0001, y=0.74x + 0.50. Analysis of agreement was as follows: 0.14 ± 0.87 cm^2 and 0.18 ± 0.83 $cm,^2$ respectively. When comparing MVA's obtained by APE and from surface rendered images, we found a good correlation: r=0.83, p<0.001, y=0.85x + 0.24, agreement analysis was 0.04 ± 0.65 $cm.^2$

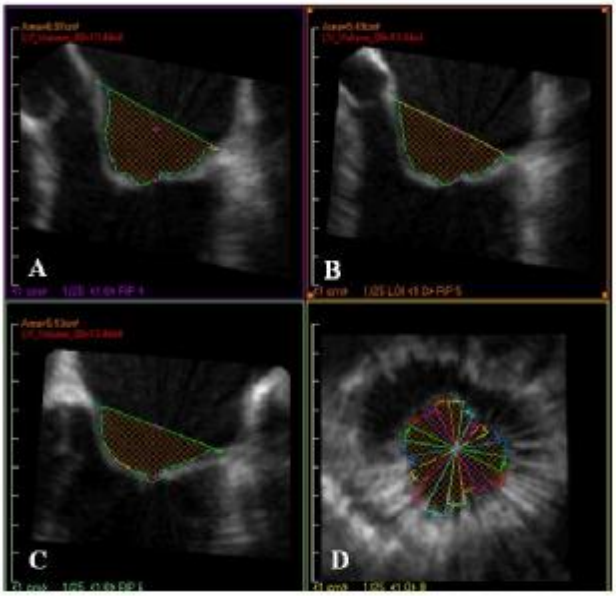

Figure 3 *Mitral valve doming volume measurement. The average rotation method with 10 slices (3 of them are presented in A, B and C) was used for generation of long axis views through the mitral apparatus. In each of them the area subtended by the anterior and posterior mitral valve as well as annular cut plane was planimetred. The volume of each slice was summed up and finally the doming volume was calculated (D).*

Mitral valve doming volume and mitral valve volume

The average doming volume was 7.11 ± 2.84 ml and mitral valve volume 2.37 ± 2.81 ml. Intra- and interobserver variability of mitral valve doming volume measurement was low (mean difference 0.04 ± 2.01 ml, 0.09 ± 2.32 ml, respectively), coefficient of variation: intraobserver 13 %, interobserver 30 %. The variability of mitral valve volume measurement was: mean intraobserver difference 0.04 ± 1.64 ml, coefficient of variation 35 %, mean interobserver difference 0.15 ± 1.07 ml, coefficient of variation 18 %.

Mitral valve stenosis and atrial fibrillation

Analysing the patients with atrial fibrillation and sinus rhythm, there was no significant difference in MVA's assessed by the PHT method (p=0.79) and APE (p=0.23). Multiple linear regression analysis showed a relation of atrial fibrillation to the doming volume (p=0.04), but not to PHT-derived MVA (p=0.28), APE-derived area (p=0.33) and mitral valve volume (p=0.08). The regression equation was: rhythm = 0.78 – 0.40 PHT area + 0.33 APE area – 0.07 doming volume + 0.06 mitral valve volume.

Mitral valve stenosis and associated valvular abnormalities

Associated valvular regurgitation had no effect on the MVA measurements carried out by Doppler PHT and 3DE. In patients with and without aortic regurgitation, there was no difference in Doppler PHT-derived MVA's and 3DE MVA's (p=0.4 and p=0.07, respectively). One patient was excluded from the analysis using PHT derived MVA's because of severe aortic insufficiency. Similarly, there was no significant difference between patients with mild mitral regurgitation and moderate to severe

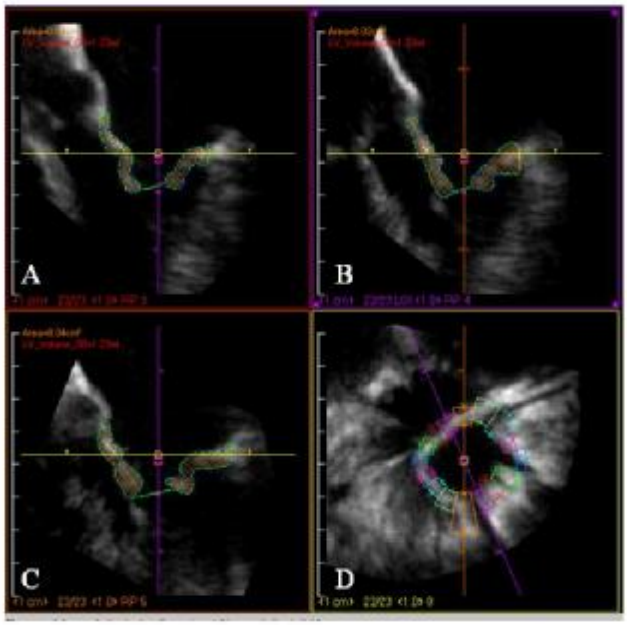

Figure 4 *Mitral valve volume measurement. Around the centre axis of the mitral valve, 8 slices (3 of them are presented in A, B and C) were generated. The boundaries of the anterior and posterior leaflets were traced and the mitral valve volume was calculated by summing the corresponding subvolumes (D).*

regurgitation graded as 2+ and 3+ in both PHT measurements and 3DE measurements (p=0.3 and p=0.6, respectively).

Critical mitral valve stenosis

Comparison of patients with (MVA < 1 cm^2) and without (MVA > 1 cm^2) critical mitral stenosis, revealed significant difference in the mitral valve volume: the mean mitral valve volume of critical stenosis was 3.7 ml and non-critical stenosis was 1.4 ml (p=0.04).

In contrast, there were no significant differences in doming volume in patients with critical and non-critical stenosis (mean doming volume in critical stenosis was 7.6 ml and non-critical stenosis 6.7 ml, p=0.4).

DISCUSSION

The discharge properties of the mitral valve, which determine the hemodynamic and clinical features of mitral valve stenosis, depend on the area and shape of the valve.[7] MVA can be determined by different echocardiographic methods.[8] These 2DE and Doppler measures of the valvular area have been validated, each has specific advantages and limitations.[9-12] 3DE by providing the possibility of computer slicing to generate any desired cross section of the mitral valve independently of physically dictated ultrasound windows, allows accurate and reproducible measurement of the MVA.

Firstly, we used two conventional methods of 3DE for the assessment of the valve area. The data were compared with the PHT-derived areas obtained by Doppler examination. Moderate correlations between 3DE and PHT-derived MVA's were found. Similar studies were conducted by Chen et al.[13] and Kupferwasser et al.,[14] in which besides the Doppler PHT method, invasive measurements were also used as a reference. Contrary to our results, high accuracy was achieved in MVA calculations by 3DE when compared with PHT-derived data. In addition, the above studies have proved that beam malalignment and difficulty with locating the mitral leaflet tips precisely by 2DE can be obviated by APE. The major limitation of our study as well as the above studies is the use of the Doppler PHT method as a reference. It is widely recognized that relatively large errors may occur with this method. In the presence of aortic regurgitation, the PHT method tends to overestimate the MVA determined at catheterization by the Gorlin formula[15,16] or the areas obtained by planimetry.[17,18] Associated valvular abnormalities in our study had no effect on PHT and 3DE measurements, however, the majority of patients had only mild aortic or mitral regurgitation (only 1 patient had severe aortic insufficiency and 2 patients severe mitral regurgitation). The PHT method is also unreliable in the setting of atrial fibrillation[19] and increased left ventricular stiffness.[20] Moreover, the PHT method calculates the effective orifice area, whereas 3DE determines the anatomic area. To date, only Kasliwal et al.[21] has compared the MVA by 3DE with the true mitral orifice in patients who underwent mitral valve replacement. A close correlation was found between the MVA measured at surgery and that calculated by 3DE (r=0.95).

Secondly, we studied two new quantitative indices for the evaluation of mitral valve stenosis: the mitral valve doming volume and mitral valve volume. Laws of fluid dynamics predict that the shape of the orifice influences its discharge. It is well known that some patients with the same anatomic MVA can be asymptomatic, whereas others may be dyspnoic. It has been shown that pressure gradient and flow through the stenotic valve depends not only on the cross sectional anatomic area but also on the three-dimensional geometry of the stenotic valve. A more conical and funnel-like valve produces a lower pressure gradient than an immobile valve with flat geometry. These variations can cause differences of up to 40% in the pressure drop for any given anatomic area.[22] In order to quantify the mobility and three-dimensional geometry of the mitral valve, we measured the doming volume, i.e., the volume subtended by the mitral valve leaflets and annular cut plane. To our knowledge, there are no previous reports on the mitral valve doming volume computation. The revealed negative relation of atrial fibrillation to the doming volume suggests that patients with more mobile mitral valves and conical geometry are likely to be on sinus rhythm, however, patients with immobile valves and flat geometry are likely to have atrial fibrillation. Hence, an etiologic relation between atrial fibrillation and leaflet geometry can be speculated. Furthermore, we assessed the volumes of the mitral valve itself. Comparison of patients with critical and

without critical stenosis, revealed significantly larger valve volumes in case of critical stenosis (3.7 versus 1.4 ml, $p<0.04$). Contrary to the study by Limbu et al.,[5] we did not find any association between atrial fibrillation and mitral valve volume.

Different 2DE methods have been proposed for the analysis of the mitral valve morphology before balloon valvuloplasty.[23,24] These scoring methods are semiquantitative and based on 2DE. The above mentioned 3DE indices, such as the doming volume and mitral valve volume, might provide quantitative indices of predicting success following balloon valvuloplasty, i.e., the leaflet mobility and thickness. However, in this study we did not analyze the relation between mitral valve scores and 3DE indices, in a study recently reported by our group, Lanegerveld et al., we found an inverse relation between the mitral valve volume and a successful balloon valvuloplasty. The mitral valve volume was not related to the Wilkins score and thickness of the mitral valve.[25]

Further developments in 3DE ultrasound instrumentation and computer technologie will lead to widespread routine applications, faster and/or real-time acquisition, processing and reconstruction and easier and versatile approaches to quantitative analysis.[26]

CONCLUSIONS

The present study confirms the moderate correlation between MVA's assessed by APE and 3DE surface rendering when compared to Doppler PHT-derived areas. We have described a new index, the doming volume, which allows quantification of the mobility and three-dimensional geometry of the mitral valve. Patients with a flat geometry of the mitral valve have a propensity to atrial fibrillation. Mitral valve volume can be used for quantitative evaluation of mitral stenosis and tends to be greater in patients with critical stenosis.

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Chapter 3

ADDITIONAL VALUE OF THREE-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY FOR PATIENTS WITH MITRAL VALVE STENOSIS UNDERGOING BALLOON VALVULOPLASTY

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ABSTRACT

The objective of this study was to validate the additional value of 3-dimensional (3D) transesophageal echocardiography (TEE) for patients with mitral valve stenosis undergoing percutaneous mitral balloon valvotomy (PTMV). Therefore, in a series of 21 patients with severe mitral valve stenosis selected for PTMV, 3D TEE was performed before and after PTMV. The mitral valve area was assessed by planimetry pre- and post-PTMV; the mitral valve volume was assessed and attention was paid to the amount of fusion of the commissures. These results were compared with findings by 2-dimensional transthoracic echocardiography using pressure half-time method for assessment of mitral valve area, and were analyzed for the prediction of successful outcome. Pre-PTMV the mitral valve area assessed by 3D TEE was 1.0 ± 0.3 cm^2 vs 1.2 ± 0.4 cm^2 assessed by 2-dimensional transthoracic echocardiography ($P = .03$) and post-PTMV it was 1.8 ± 0.5 cm^2 vs 1.9 ± 0.6 cm^2 (not significant), respectively. The mitral valve volume could be assessed by 3D TEE (mean 2.4 ± 2.5 cm^3) and was inversely correlated to a successful PTMV procedure ($P < .001$). The 3D TEE method enabled a better description of the mitral valvular anatomy, especially post-PTMV. We conclude that 3D TEE will have additional value over 2-dimensional echocardiography in this group of patients, for selection of patients pre-PTMV, and for analyzing pathology of the mitral valve afterward.

INTRODUCTION

Percutaneous mitral balloon valvotomy (PTMV) has proven to be an effective method of treatment for patients with mitral valve stenosis (MVS).[1-8] The selection of PTMV relies on the morphologic changes of the rheumatic mitral valve and its hemodynamic effects. Two-dimensional (2D) transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) play a crucial role in this selection[9] and they are helpful for the prediction of good functional short-[3,4,10,11] and long-term results.[4,10,12]

Three-dimensional echocardiography is a recently developed, evolving imaging technique that allows visualization of intracardiac structures from any perspective. This offers additional unique advantages. Quantitative 3D echocardiography can be applied for the measurement of the mitral valve area (MVA) by planimetry and for the mitral valve volume (MVV) in vivo.[13] The 3D echocardiographic reconstruction enables visualization of the mitral valve so that commissural splitting and leaflet tears after PTMV, not seen with 2D echocardiography, become visible.[14] The usefulness of this 3D imaging technique in selecting patients for PTMV and in examining the effects of balloon valvuloplasty on the mitral valve after PTMV needs further investigation.

Therefore, in a series of patients with severe MVS selected for PTMV, subsequent qualitative and quantitative evaluation of the mitral valve before and after PTMV was performed by 3D TEE. These results were compared with findings by 2D TTE and were analyzed for the prediction of successful outcome.

METHODS

Patient selection

All patients in this prospective study were selected for PTMV by medical history, physical examination, and 2D echocardiography (TTE and TEE), showing symptomatic and severe MVS. Patients gave informed consent for performing 3D TEE before and 3 months after PTMV.

Examination by 2D TTE

Acquisition of 2D TTE images and continuous wave Doppler was performed with a transthoracic, 2.5-MHz, phased-array transducer connected to an ultrasound system (Sonos 1500 or 2500, Hewlett-Packard, Andover, Mass). Examination by 2D TTE was performed before, within 24 hours, and 3 months after PTMV. Valvular and subvalvular lesions were assessed by this technique pre- and post-PTMV and the Wilkins score was determined.[9] The short-axis view of the mitral valve, obtained from the left parasternal window, was used to examine the mitral commissural morphology. Commissural splitting was graded at each side using a score of 0 to 2. Grade 0 indicated no fusion of the commissure; grade 1, a moderate fusion; and grade 2, a complete fusion.

The Doppler technique was used with continuous wave recordings to calculate the maximal and mean transvalvular gradient and to assess the MVA by the transmitral pressure half-time index (PHT) index.[15] Color Doppler echocardiography was used to detect atrial shunts and mitral regurgitation.

Examination by 2D TEE

Two-dimensional TEE was performed at the referring hospital. Special attention was paid to the presentation of thrombi in the left atrium or left atrial appendage, which is an exclusion criteria for PTMV. In none of the study patients was a thrombus found.

Table 1 Characteristic of patients at baseline

	N	%
Patients	21	
(women)	16	76.2
Age (y) (mean ± SD)	49 ± 15	
Previous PTMV	1	5
Surgical commissurotomy	1	5
NYHA class		
II	8	38.1
III	13	61.9
Rhythm		
Sinus rhythm	10	47.6
Paroxysmal AF	8	38.1
Chronic AF	3	14.3
CAG	13	61.9
Normal vessels	13	100

AF, Atrial fibrillation; CAG, coronary angiography; NYHA, New York Heart Association; PTMV, percutaneous mitral balloon valvotomy.

Examination by 3D TEE

Examination by 3D TEE was performed before and 3 months after PTMV. Acquisition of 3D TEE was performed with a 5-MHz multiplane TEE transducer connected to an ultrasound system (Sonos 2500 or 5500, Hewlett-Packard). Rotational acquisition was performed (stepwise 2 or 3 degrees), with electrocradiogram and respiratory gating. The 3D data were stored on a magneto-optical disk. The recorded images were processed offline on a workstation (TomTec, Version 4.0, Tom Tec Imaging System, Munich, Germany), where the raw data were converted into a volumetric data set.

Anyplane echocardiography was used for MVA measurement. In this model, 2 long-axis views and 1 short-axis view through the mitral valve were defined (Figure 1). These cut planes were nearly perpendicular to each other. The position of the short-axis cut plane along the long axis was indicated through the lines of intersection and displayed in the reference image. The position of displayed short-axis cut plane was further adjusted by the guidance of the line of intersection display. The image that cut the

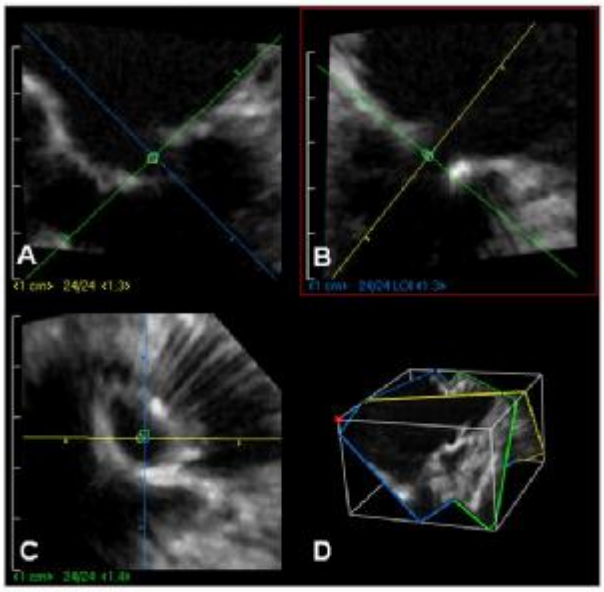

Figure 1 *Mitral valve area measurement using anyplane echocardiography. Two long-axis cut planes perpendicular to each other (**A** and **B**). By guidance of line of intersection, optimal short-axis cut plane was selected (**C**). 3D data set and spatial alignment of 3 cut planes (**D**).*

mitral valve just at the cusp tips was selected for area measurement by planimetry. This was the smallest anatomic area of the mitral valve.[16,17]

The boundary tracing method was used for volume computation of the mitral valve leaflets, as described by Limbu et al.[13] A software package (LVCAP, Version 1.0, TomTec, Version 4.0, Tom Tec Imaging System, Munich, Germany) implemented in the workstation system was used for these volume calculations. An average rotation method with 8 slices was used (Figure 2). The central axis of the mitral apparatus, around which the slices were constructed, was selected by the guidance of the line of intersection display. Consequently, the end-diastolic phase was selected on the basis of the R wave of electrocardiogram, to visualize the clear boundaries of mitral valve leaflets. The boundaries were traced by the mouse-driven cursor. After the volume of each slice had been calculated, the system summed the corresponding subvolumes and finally calculated the volume of the whole mitral valve. In addition, volume rendering of the mitral valve was performed from the left atrium.

The commissural morphology was analyzed in 3D volume-rendered images. The opacity and threshold settings were optimized by increasing their values until artifacts had appeared within the body of the leaflets. The optimal viewing cut plane was selected so that the commissural morphology was best visualized. Attention was paid to the morphology of the mitral valve pre- and post-PTMV, with special attention to commissural splitting, leaflet tears, or chordal rupture. Commissural splitting was graded at each side using a score of 0 to 2, as explained previously.

PTMV procedure

PTMV was performed by the anterograde, transseptal approach with the Inoue balloon catheter (Toray Industries, Tokyo, Japan) (n = 18).[18] In 3 patients the multitrack

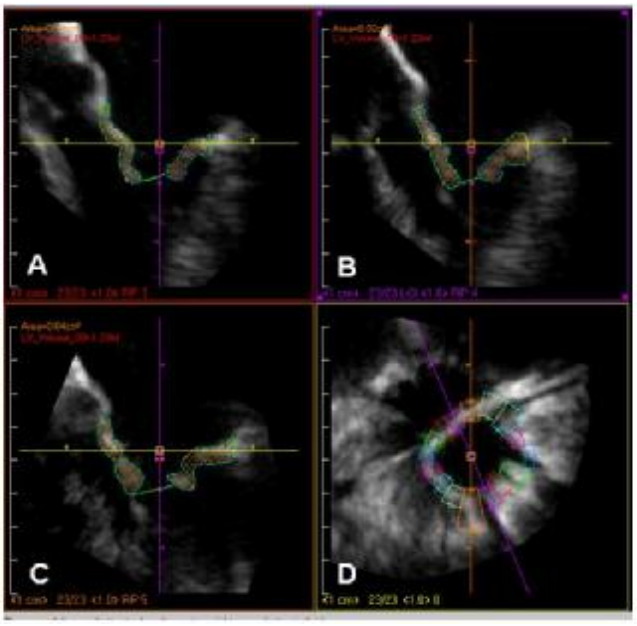

Figure 2 *Volume measurement of mitral valve leaflets by anyplane echocardiography. Three long-axis cut planes constructed around center axis of mitral apparatus (**A**, **B**, and **C**). In these views boundaries of mitral valve subvolumes were traced and their corresponding short-axis views are presented in short-axis cut plane (**D**). In all, 8 slices were used for volume computation.*

system was used.[19] A successful procedure was defined as a MVA 1.5 cm^2 (2D TTE) after PTMV and no severe mitral valve regurgitation (grade III/IV).

Statistical analysis

Data were expressed as mean ± SD; reduced sample sizes are indicated. The Fisher exact test was used for comparing categoric variables. For comparison of continuous variables the Student t test was used, or the Mann-Whitney test where appropriate. A P value < .05 was considered statistically significant.

The correlation between MVA values obtained by 2D TTE and 3D TEE pre- and post-PTMV was assessed by linear regression analysis. Agreement between these 2 MVA measurements was assessed as described by Bland and Altman.[20]

To determine the intraobserver variability for MVV measurements by 3D TEE, the same observer repeated measurements a few months later, without reference to the previous measurements. To determine the interobserver variability, in 10 patients a second observer, who was blinded for the measurements of the first observer, assessed the MVV. The intraobserver and interobserver variability was assessed by the Student t test. Agreement between the 2 MVV measurements by the same observer and by 2 different observers was assessed as described by Bland and Altman.[20]

RESULTS

Patients

A total of 21 consecutive patients (5 men and 16 women, age 49 ± 15 years, range 18 to 70 years) undergoing PTMV were prospectively enrolled. All clinical patient data before PTMV are summarized in Table 1.

Echocardiographic data pre-PTMV

Data by 2D TTE. Table 2 summarizes the echocardiographic data by 2D TTE of the patients pre-PTMV. It was possible to describe the fusion of the commissures in 19 of 21 patients (90%) (Table 3).

Data by 3D TEE. The mean MVA at baseline, measured by 3D TEE, was 1.02 ± 0.29 cm^2 (n = 20). The image quality was not sufficient in 1 patient to assess the MVA. The commissures could be described in 18 of 19 patients (95%) (Table 3). In 2 patients the 3D data of the commissures were lost.

The MVV could be assessed in all patients (n = 20). In 1 patient the 3D data of MVV were lost. The mean MVV was 2.4 ± 2.5 cm^3 (range: 0.7-12.0 cm^3). The differences between the 2 measurements by the same observer were not statistically significant (P = .83).

The correlation coefficient between these measurements was 0.97. The Bland-Altman graph showed the distribution of differences to be within 2 SD for all values, except for 1, with a mean value of 0.04 ± 0.84 cm^3. The mean MVV assessed by a second observer was 2.9 ± 3.6 cm^3 (range: 0.8-12.7 cm^3)(n = 10). This value was not statistically significantly different compared with the mean MVV assessed by the first observer in these 10 patients (mean MVV 3.0 ± 3.5 cm^3) (P = .61). The correlation coefficient between these values was 0.99. The Bland-Altman graph showed the distribution of differences to be within 2 SD for all values, with a mean value of 0.07 ± 0.44 cm^3.

The MVV was not significantly related to the Wilkins score, the thickness of the mitral valve, age, sex, New York Heart Association class pre-PTMV, rhythm, MVA (2D TTE), or the amount of mitral regurgitation pre-PTMV.

Comparison of 2D TTE and 3D TEE. The MVA measured by 3D TEE (planimetry) was statistically significantly smaller compared with the MVA by 2D TTE (PHT index) (P = .03, n = 20). The correlation between both methods is shown in Figure 3, A (r = 0.62). The corresponding Bland-Altman plot, showing a mean difference of 0.15 ± 0.29 cm^2 between the 2 methods, is shown in Figure 3, B.

In 11 of 18 patients (61%) the grade of fusion of the anterolateral commissure and in 8 of 18 patients (44%) the grade of fusion of the posteromedial commissure was overestimated by 2D TTE compared with 3D TEE (Table 3).

PTMV procedure

PTMV was fulfilled in all patients. A hemopericardium developed in 2 patients during the procedure, which needed pericardiocenthesis. There were no embolic events or vascular complications. One patient needed mitral valve replacement at 2 months after PTMV because of severe mitral regurgitation.

Table 2 Echocardiographic results before and after percutaneous mitral balloon valvotomy by 2-dimensional transthoracic echocardiography

	Pre-PTMV N = 21 mean ± SD	Post-PTMV ≤ 24 h N = 21 mean ± SD	Post-PTMV 3 mo N = 12 mean ± SD
MV area (cm2)	1.18 ± 0.36	1.91 ± 0.57*	1.90 ± 0.56*
MV max gradient (mm Hg)	18.1 ± 4.9	11.8 ± 3.2*	11.1 ± 2.8*
MV mean gradient (mm Hg)	9.8 ± 3.6	5.7 ± 2.3*	5.2 ± 1.7*
Wilkins score	6.3 ± 1.4		
	N (%)	N (%)	N (%)
MV regurgitation grade			
0	10 (47.6)	1 (4.8)	2 (16.7)
I	9 (42.9)	10 (47.6)	3 (25.0)
II	2 (9.5)	9 (42.9)	7 (58.3)
III		1 (4.8)	

max, Maximal; MV, mitral valve; PTMV, percutaneous mitral balloon valvotomy. Mitral valve area is assessed by pressure half time method.

**Significant different compared with pre-PTMV (P < .01)*

Echocardiographic data immediately post-PTMV

Data by 2D TTE. Table 2 summarizes the echocardiographic data by 2D TTE immediately post-PTMV (24 hours). The final valve area was 1.5 cm^2 in 18 patients (85.7%). The initial success rate of PTMV was 81.0% (17 of 21 patients).

Successful procedure

Data by 2D TTE. The MVA pre-PTMV assessed by 2D TTE was significantly related to a successful PTMV procedure (P = .049). The maximal mitral valve gradient, the mean mitral valve gradient, the fusion of the commissures, the amount of mitral valve regurgitation, and the Wilkins score were not significantly related to a successful procedure.

Data by 3D TEE. The MVA pre-PTMV assessed by 3D TEE was not significantly related to a successful PTMV procedure. However, the MVV pre-PTMV

was significantly related to a successful procedure ($P < .001$). The mean MVV in patients with a successful procedure was 1.5 ± 0.5 cm^3 (n = 16) and, in patients with a nonsuccessful procedure, 5.8 ± 4.3 cm^3 (n = 4), with a cut-off point of 2.5 cm^3. The amount of fusion of the commissures was not significantly related to a successful procedure.

Table 3 Fusion of anterolateral and posteromedial commissure before and after percutaneous mitral balloon valvotomy

Fusion grade	Pre-PTMV		Post-PTMV	
	2-D TTE	3-D TEE	2-D TTE	3-D TEE
0	0	1	5	9
1	0	10	3	3
2	19	7	0	0
?	2	1	4	0
Fusion grade	Pre-PTMV		Post-PTMV	
	2-D TTE	3-D TEE	2-D TTE	3-D TEE
0	0	1	4	10
1	5	9	3	2
2	14	8	1	0
?	0	1	4	0

PTMV, Percutaneous mitral balloon valvotomy; TEE, transesophageol echocardiography; TTE, transthoracic echocardiography; 2-D, 2-dimensional; 3-D, 3-dimensional.

0 = No fusion; 1 = moderate fusion; 2 = severe fusion; ? = image quality not sufficient. Upper section = anterolateral; lower section = posteromedial.

Echocardiographic data three months post-PTMV

At 3 months post-PTMV, 3D TEE was performed in 12 patients (57%). In 9 patients this postprocedural 3D TEE was not performed: 8 patients (38%) refused; and in 1 patient (5%) the mitral valve was replaced at 2 months after PTMV. All these 12 patients also underwent 2D TTE at 3 months post-PTMV. We will discuss the echocardiographic results of these 12 patients.

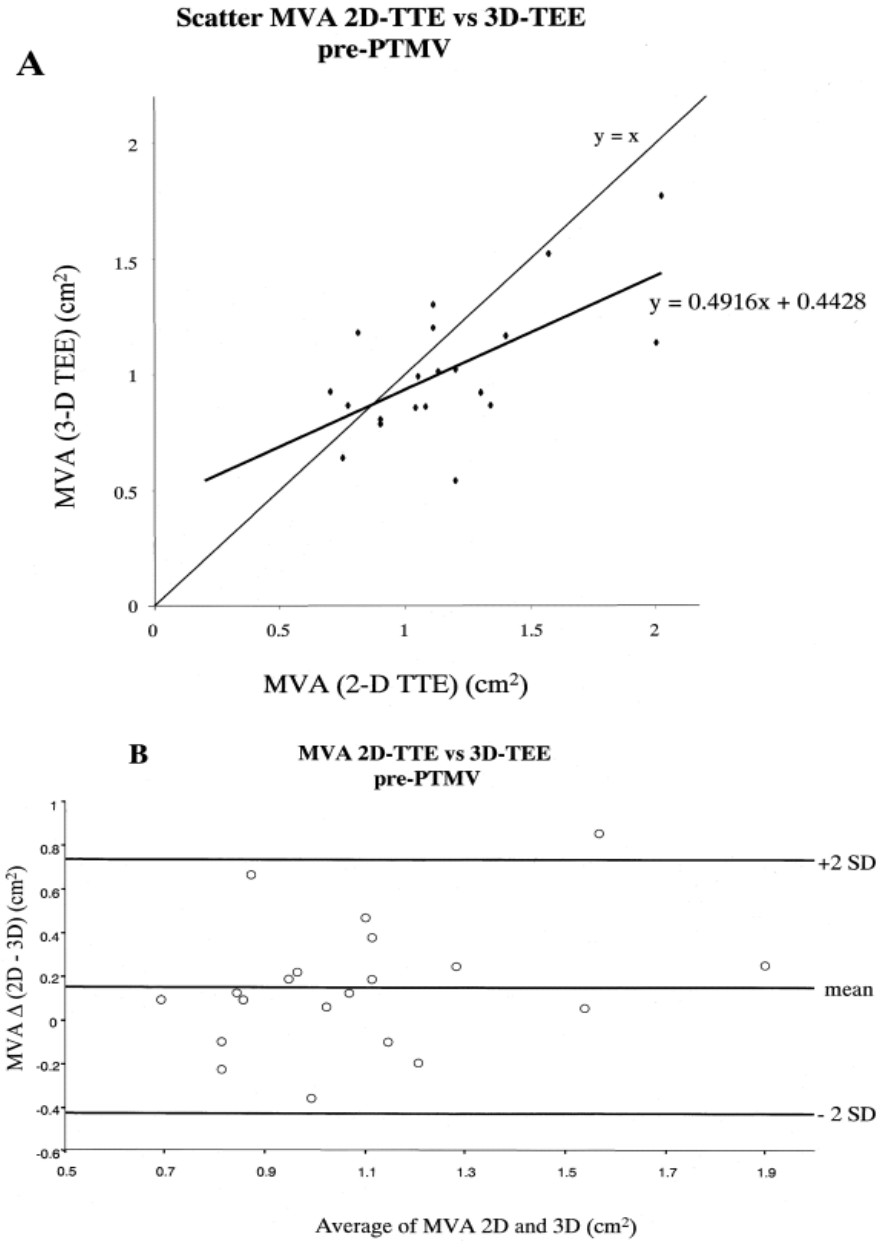

Figure 3 *Scatter plot showing correlation between mitral valve area (MVA) pre-percutaneous mitral balloon valvotomy (PTMV) estimated by 2-dimensional transthoracic echocardiography (pressure half-time) and by 3-dimensional transesophageal echocardiography (planimetry) (**A**). Corresponding Bland-Altman plot is added (**B**) (n = 20).*

Data by 2D TTE. Table 2 summarizes the echocardiographic data by 2D TTE at 3 months post-PTMV. Description of the commissures was possible in 8 of 12 patients (67%) (Table 3). In all these 8 patients the grade of fusion of the commissures decreased after PTMV. In 4 patients (33%) the commissures could not be visualized because of poor image quality. In 1 patient a tear was seen in the posterior mitral valve.

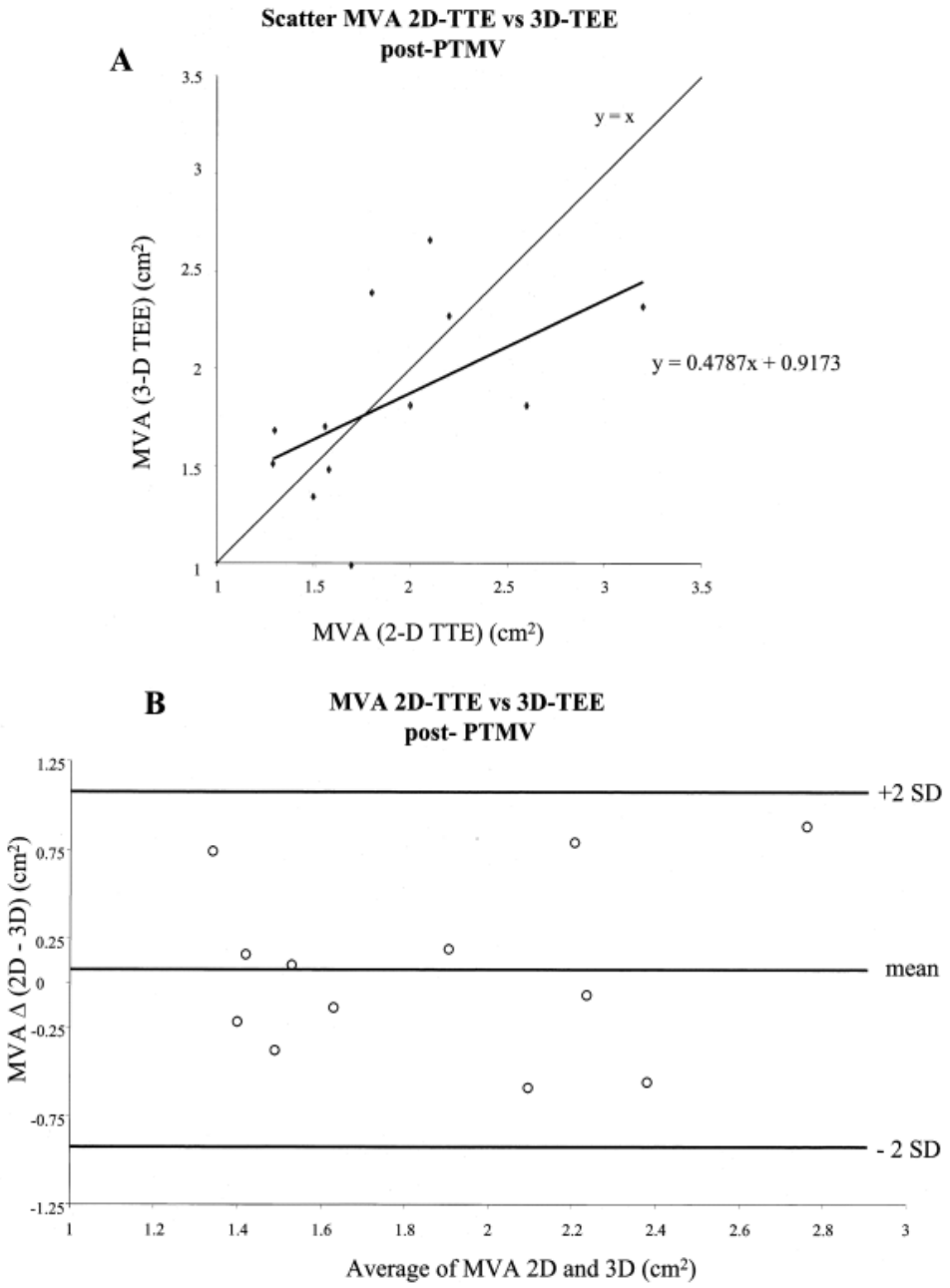

Figure 4 *Scatter plot showing correlation between mitral valve area (MVA) post-percutaneous mitral balloon valvotomy (PTMV) estimated by 2-dimensional transthoracic echocardiography (pressure half-time) and by 3-dimensional transesophageal echocardiography (planimetry)* ***(A)****. Corresponding Bland-Altman plot is added* ***(B)*** *(n = 12).*

Data by 3D TEE. The mean MVA measured by 3D TEE at 3 months was 1.83 ± 0.49 cm^2 (n = 12). This was significantly improved compared with the MVA measured pre-PTMV (mean difference 0.71 ± 0.41 cm^2, P < .01).

Description of the commissures was possible in all 12 patients by 3D TEE (Table 3). In 1 patient (with a successful procedure), splitting in none of the commissures occured after PTMV. In all other patients, at least 1 commissure had the grade of fusion decreased after PTMV. In 2 patients a tear was seen in the posterior mitral valve.

Comparison of 2D TTE and 3D TEE. The MVA assessed by 3D TEE post-PTMV was not significantly different compared with 2D TTE post-PTMV (n = 12). The correlation between both methods is shown in Figure 4, A (r = 0.55). The corresponding Bland-Altman plot showing a mean difference of 0.08 ± 0.51 cm^2 between the 2 methods is shown in Figure 4, B.

In 5 of 8 patients (63%) the fusion of the anterolateral commissure and in 4 of 8 patients (50%) the fusion of the posteromedial commissure described by 3D TEE equals the description by 2D TTE. In only 1 of the 2 patients with a tear in the posterior mitral valve seen by 3D TEE, was this tear also seen by 2D TTE.

DISCUSSION

This study shows that in a consecutive group of patients with MVS treated by PTMV, 3D TEE can safely be performed pre-PTMV and at 3 months later. Pre-PTMV assessment of MVV by quantitative 3D TEE is possible and reproducible, and is correlated to a successful PTMV procedure. Post-PTMV, 3D TEE improves the description of the valvular anatomy, in particular compared with 2D TTE. The number of patients in this study is low, therefore, we should be cautious to draw conclusions for all patients with MVS.

Mitral valve area

Assessment of the MVA is important for the classification of severity of MVS, for the estimation of success of PTMV, and for follow up after this procedure. In many studies, MVA is assessed by Doppler echocardiography, using the PHT method.[15,21-23] This is an indirect measurement and is influenced by hemodynamic variables.[24-28] By planimetry, a direct measurement of the mitral valve orifice can be performed.[29,30] However, this method is limited to those patients in whom images of good quality can be obtained in the parasternal short-axis window, thus, considerable experience and operator skill are necessary.[31]

Recently it has been demonstrated that 3D echocardiography provides accurate and reproducible measurements of MVA by planimetry.[16,17,31] In the 3D data set, cross-sectional images of the mitral valve can be generated in any plane desired, independently from orientations dictated by the acoustic windows, and this allows more accurate measurement of the orifice area in patients with MVS.[17] In only 1 published study was the MVA measured both pre-valvuloplasty and post-valvuloplasty by 3D TEE.[14]

In our study we found that, pre-PTMV, the MVA derived by 3D TEE was 0.15 cm^2 smaller compared with the MVA derived by 2D TTE. This difference was statistically significant (P = .03). However, clinically, this difference is not meaningful. Post-PTMV, we found that the MVA assessed by 3D TEE was not statistically significantly different compared with the MVA assessed by 2D TTE. Also, others did not find significant differences between MVA values derived by 3D TEE and those obtained by Doppler PHT method pre-[14,17,31] or post-PTMV.[14] The assessment of MVA by 3D TEE requires much experience and this method is labor- and time-intensive, whereas the PHT method is easy to perform. Therefore, we think there is no role for an assessment of MVA by 3D TEE pre- or post-PTMV routinely. However, for patients with a bad

acoustic window or when the PHT method is not reliable,[26,27,28] MVA assessed by 3D TEE can be a valuable alternative. This hypothesis needs further investigation with a larger number of patients.

Mitral valve volume

MVS is a progressive disease associated with progressive morphologic changes of the mitral valve and the subvalvular structures. The selection for PTMV relies on these morphologic changes and the hemodynamic consequences. In many studies the echocardiographic Wilkins score[9] has been a significant predictor for success or failure of the PTMV procedure.[3,4,10,11,32] Limbu et al[13] described the volume assessment of the mitral valve by 3D TEE. We analyzed the predictive value of this new morphologic score for a successful PTMV procedure.

In our study, the MVV could be assessed in all patients pre-PTMV. The intraobserver variability and the interobserver variability was acceptable; the corresponding correlation coefficient was excellent; and the Bland-Altman curve showed, on average, a good agreement between the measurements. The MVV pre-PTMV was significantly and inversely related to a successful PTMV procedure. We even found a cut-off point for the MVV of 2.5 cm^3 to predict a successful procedure.

Limbu et al[13] found that the MVV could satisfactorily be measured by 3D echocardiography. The volumes they mentioned were larger than the volumes mentioned in our study. Probably this is caused by the fact that the procedure is not yet standardized. For the accurate measurement of the MVV, good echocardiographic image quality is important. This depends on the threshold settings and the reconstruction algorithms used. The chosen cut plane is also important for an accurate measurement of MVV. The indefinite outlines of the mitral valve annulus will be a cause of error in the measurement.

We think there will be a role for MVV assessment for the selection of patients for PTMV. However, a more standardized procedure of MVV measurement is needed as are further studies with larger number of patients to define the exact role of MVV assessment in clinical practice.

The potential value of 3D TEE for analyzing the mitral valve anatomy and especially for detecting postinterventional complications

Visualization of mitral valve morphology by 2D TTE is possible, however, the assessment of the commissural, leaflet, and subvalvular morphology is limited to those patients in whom images of good quality can be obtained. However, when precordial imaging is optimal, detailed anatomic analysis is often not possible. By anyplane 3D TEE, the cut planes are unrestricted, allowing a detailed analysis of the mitral valve apparatus.[33] By 3D volume-rendered echocardiography, dynamic 3D reconstructions can be performed of the mitral valve structure en face of either a left atrial or a left ventricular perspective, including detailed visualization of the commissures, leaflets, and subvalvular structures.[33] Salustri et al[33] found 3D volume-rendered echocardiography to be superior to 2D echocardiography for the evaluation of commissures.

In our study, pre-PTMV, the commissures could be described in almost all patients by 2D TTE (90%) and by 3D TEE (95%). However, the amount of fusion was overemphasized by 2D TTE compared with 3D TEE in almost half the patients. Postprocedurally, the commissures could be described in all patients by 3D TEE, whereas by 2D TTE this was possible in 67% of patients. In all but 1 patient splitting of

the commissures has occurred after PTMV (3D TEE). In addition, Applebaum et al[14] found, by 3D TEE, splitting of the commissures to occur in all patients after PTMV.

In 2 patients a tear was seen in the posterior mitral valve by 3D TEE post-PTMV. In 1 of them this tear was also seen by 2D TTE. We should be cautious with these observations, because it is easy to create an echocardiographic dropout by changing the gain setting or the level of threshold.[14] However, Applebaum et al[14] found 3D TEE to be helpful for detecting leaflet tears. In their study, leaflet tears were visualized in 38% of patients when an increase in mitral regurgitation–complicated PTMV.

Our findings suggest that 3D TEE improves our information about the commissural and leaflet morphology pre- and post-PTMV and can be helpful in detecting complications postprocedurally. However, the gold standard for the assessment of commissural and leaflet morphology is by visualization at the time of operation or postmortem. Therefore, we do not know the validity of our observations by 3D TEE.

Limitations and perspectives of 3D TEE

Three-dimensional echocardiography is time-consuming and labor-extensive. The preparation of the investigation takes more time than conventional TTE or TEE. Most time is spent postprocedurally.[34] In some instances, for more than 1 hour. Therefore, it is still impractical for routine clinical use. Binder et al[31] presented a promising study about transthoracic volumetric real-time 3D echocardiography. This echocardiography technique can be performed in a few minutes, because of the instant acquisition of the complete 3D data set without complex postprocessing, and the measurements are simple.[31] It is not transesophageal and, therefore, causes less discomfort. However, this new imaging technique needs further investigation.

Three-dimensional echocardiography is susceptible to reconstruction artifacts.[14,34] It is extremely sensitive to proper gain settings from the 2D data acquisition and to the level of threshold chosen during the 3D reconstruction.[14] An inappropriate setting of either modality can result in an ultrasonic dropout. The image result is also influenced by the chosen cut plane, angle, and reconstruction algorithms used.[34] Therefore, more standardized procedures of measurement are needed.

Gray level information of 3D images cannot be used for tissue differentiation (calcification vs fibrosis).[35] Therefore, 3D will be of added, rather than competitive, value to 2D images.

Probably in the future there will be a role for 3D echocardiography in clinical practice of MVS, especially in patients with a bad acoustic window or when the PHT method is not reliable for the assessment of MVA. However, far more studies with larger patient populations are needed to verify this statement. Our findings about MVV are promising.

CONCLUSIONS

Three-dimensional TEE can provide additional information to 2D TTE in patients with MVS, pre-PTMV and post-PTMV. It can be a valuable alternative when MVA assessment by 2D TTE is not reliable. The MVV can be assessed by 3D TEE. The MVV is inversely correlated to a successful PTMV procedure and can possibly be useful for the selection of patients for PTMV. Post-PTMV 3D TEE improves the description of the valvular anatomy. This enables more understanding of the mechanisms of successful PTMV and its complications. Both technical improvement and larger studies are needed before the usefulness of 3D TEE in patients with MVS is clear.

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Chapter 4

QUANTITATIVE ASSESSMENT OF MECHANICAL PROSTHETIC VALVE AREA BY 3-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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ABSTRACT

Objective: The goal of this study was to assess the geometric orifice area of mechanical valve prostheses by transesophageal 3-dimensional echocardiographic planimetry.

Methods and Results: Currently used Doppler methods for prosthetic assessment (orifice area-Doppler) were compared with 3D planimetry for orifice area (orifice area-3D) and with manufacturer's values (orifice area-manufacturer) for the corresponding prosthesis types and sizes and with historical controls provided by Doppler literature (orifice area-literature). Twenty-four mechanical valve prostheses (in 22 patients) were studied: 13 in mitral position and 11 in aortic position. Orifice area-manufacturer, orifice area-Doppler, orifice area-literature, and orifice area-3D were 3.6 ± 1.1 cm^2, 2.3 ± 0.9 cm^2, 2.4 ± 0.9 cm^2, and 2.6 ± 0.7 cm^2, respectively. Orifice area-manufacturer values were significantly larger. Correlation coefficients between orifice area-3D and orifice area-manufacturer, and between orifice area-3D and orifice area-Doppler and orifice area-literature were 0.83, 0.90, and 0.73, respectively (all $P < .0001$).

Conclusion: Three-dimensional transesophageal echocardiography is feasible and has good correlation with orifice area-Doppler (in aortic position) and good correlation with orifice area-manufacturer (in aortic and mitral positions) methods.

INTRODUCTION

Currently, prosthetic valve function is mainly assessed noninvasively by 2-dimensional (2D) transthoracic and transesophageal (Doppler) echocardiography techniques from which structural and hemodynamic information is derived.[1] The current Doppler methods for effective orifice area assessment, which are based on pressure half-time (for the mitral valve prosthesis) and the continuity equation (applicable to both mitral and aortic valve prostheses), have their own known limitations.[2] Three-dimensional (3D) transesophageal echocardiography (TEE) has been introduced recently as a new ultrasonic modality for planimetric assessment of the valve area in mitral and aortic stenosis.[3,4] Prosthetic valves can be evaluated by 3D TEE for anatomic detail[5] (pannus formation) and function[5] (prosthetic valve regurgitation). No reports have been published yet regarding quantitative assessment of maximal prosthetic valve area. Therefore the aim of this study was to assess the feasibility of prosthetic orifice area measurement by 3D anyplane transesophageal echocardiography in patients with normally functioning valve prostheses in the mitral and aortic positions.

METHODS

Patients

Thirty consecutive patients with normal prosthetic function by prior transthoracic Doppler echocardiography and without clinical signs of prosthetic dysfunction were asked to participate in a 2D/3D TEE procedure in accordance with institutional guidelines and with prior informed consent. Five patients refused to undergo TEE. The mechanical valve prostheses in the aortic position could not be evaluated in 3 patients by 3D TEE because of artifacts that rendered the images technically inadequate for 3D analysis (therefore these were not included in the study results). Thus 22 patients were included, in whom 24 mechanical valve prostheses were present. Thirteen patients had a prosthetic valve in the mitral position (10 St Jude Medical [St Paul, Minn] and 3 Medtronic Hall [Minneapolis, Minn]; size range 27 to 33) and 11 patients a prosthetic valve in the aortic position (8 St Jude Medical, 1 CarboMedics [Austin, Tex], 1 Medtronic Hall, and 1 Bjork Shiley ABP [Shiley, Inc, Irvine, Calif]; size range 19 to 27). One patient with a mitral valve prosthesis was studied twice with a time interval of 4 months (to rule out endocarditis). In another patient who underwent both aortic valve replacement (AVR) and mitral valve replacement (MVR), both prostheses were analyzed. The study population consisted of 8 women and 14 men (mean age 64 years, range 41 to 77 years). The mean time between valve replacement and 3D TEE was 2.7 ± 3.7 years (range 0.02 to 15 years). All were in sinus rhythm except one patient who had atrial fibrillation. Systolic left ventricular function by 2D TEE in 22 patients was semiquantitatively scored as poor in 4 patients, moderate in 4, and good in 14.

Transthoracic Doppler and 3D TEE: Data acquisition and processing

Two-dimensional transthoracic echocardiography and Doppler echocardiography were performed and analyzed on-line with a Hewlett-Packard Sonos 2500 or 5500 system (Agilent Technologies, Palo Alto, Calif). Transthoracic Doppler of the mitral or aortic valve prosthesis was performed from acoustic windows that allowed optimal beam alignment with flow through the prosthetic valve with use of a 2- to 4-MHz transducer or a dedicated continuous-wave pencil probe. For a mitral valve prosthesis, pressure half-time was assessed with continuous-wave Doppler. For an aortic valve prosthesis, systolic velocity integrals (continuous-wave Doppler) were measured, as were the left ventricular

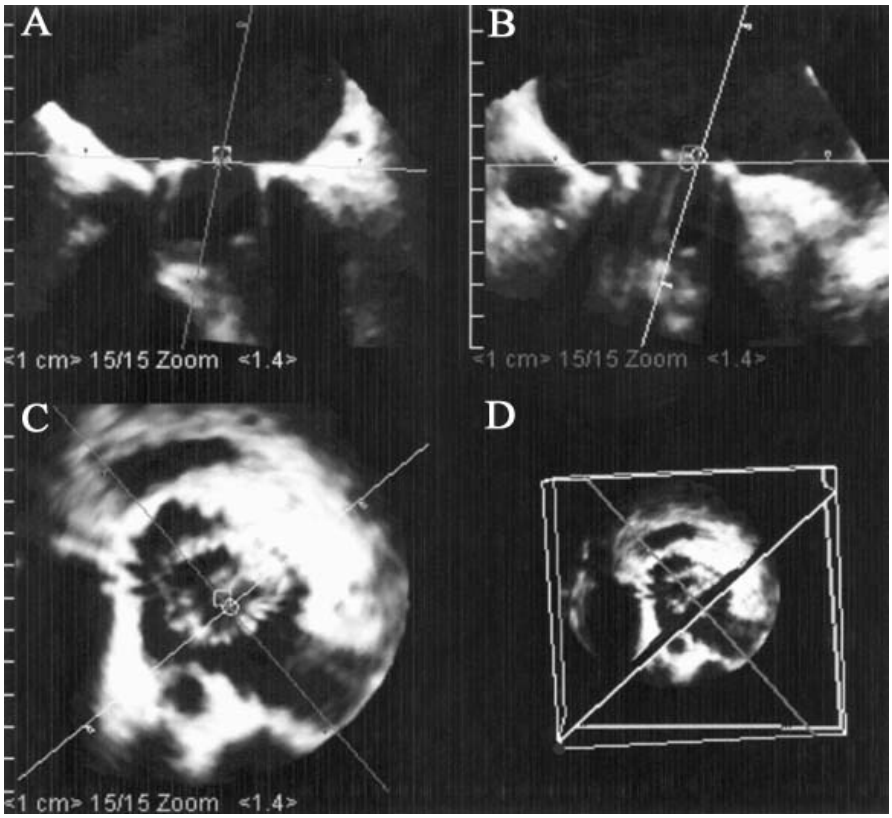

Figure 1 *This 4-tile image display window shows a St Jude mitral valve prosthesis with 2 perpendicular longitudinal-axis cut planes (**A** and **B**) obtained by anyplane echocardiography. The cut lines were positioned at the level of the inner ring of the mechanical valve at its maximum opening. Thus a true short axis of the valve orifice was derived (**C**). A reference image (**D**), in which the cut planes could be positioned freely, was helpful for adjusting, selecting, and observing the optimal cross section.*

outflow tract time-velocity integrals (pulsed-wave Doppler). The left ventricular outflow tract diameter was obtained from the parasternal long axis at the aortic annulus at maximal aortic opening. Three consecutive beats were averaged in patients in sinus rhythm, and 5 were averaged in patients with atrial fibrillation. With use of the pressure half-time and the continuity equation methods, the effective orifice areas were calculated according to standard methods published earlier.[6,7] Both will be referred to as orifice area-Doppler.

Immediately after transthoracic echocardiography, 3D TEE was performed with a 5-MHz, 64-element multiplane transesophageal transducer connected to a Hewlett-Packard Sonos 2500 or 5500 system. After the diagnostic multiplane 2D TEE, the probe was located at the esophageal level for optimal evaluation of the mitral and aortic mechanical valves. A few test runs with 180° rotation of the transducer array were performed to ensure that the prosthetic valve was encompassed centrally within the conical acquisition volume. Gain, compress, and focus settings were optimized for the prosthetic valve. Three-dimensional TEE acquisition was performed on the same ultrasonographic machine by dedicated software with 3°-interval rotation from 0° to 180° with electrocardiographic and respiratory gating, and data were stored on a magneto-

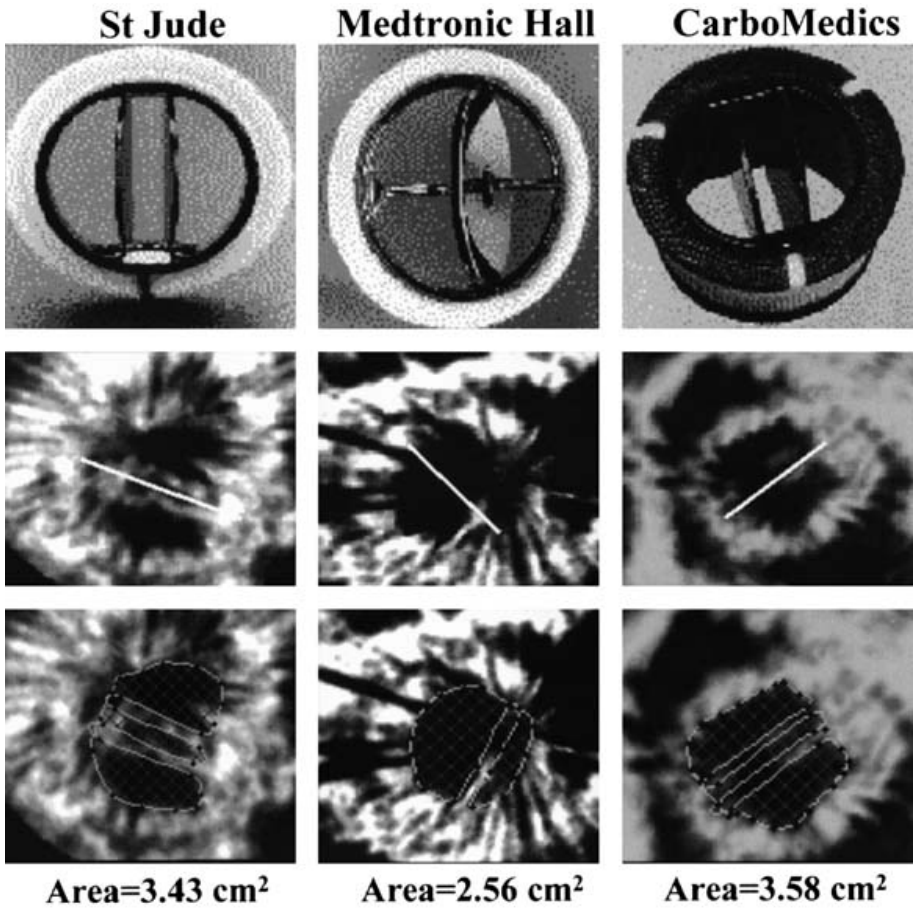

Figure 2 *Illustration of 3 types of valves used in this study (anyplane mode). The upper left panel shows a St Jude Medical valve prosthesis, the upper middle panel a Medtronic Hall valve prosthesis, and the upper right panel a CarboMedics valve prosthesis. The corresponding middle panels show the diameters measured, and the lower panels show the orifice area measurements.*

optic disk. The results of the acquisition were reviewed and replayed immediately afterwards to check for artifacts. Both 2D TEE and Doppler examinations were recorded on VHS videotape. Three-dimensional TEE data were processed off-line on a TomTec 4.1 EchoView (TomTec Imaging System Inc, Munich, Germany) system, in which the raw data were converted into a volumetric data set.

Mechanical valve orifice area measurements by anyplane 3D TEE

Three-dimensional reconstruction was performed off-line on a TomTec 4.1 EchoView workstation in a 4-tile image display window by the anyplane mode (ie, anyplane 3D TEE). The prosthetic valve size and diameter were unknown to the operator at the time of analysis. One tile was used to generate cut planes of the mechanical valve along its long axis. From this long-axis cut plane a perpendicular longitudinal plane was generated (Figure 1). From these 2 longitudinal axes an optimal short axis through the prosthetic valve was created by “line-of-intersection” navigational mode. With this mode a cut line was positioned in a plane encompassing the inner ring of the mechanical valve at its maximal opening. The optimal cross section of the valve orifice was further

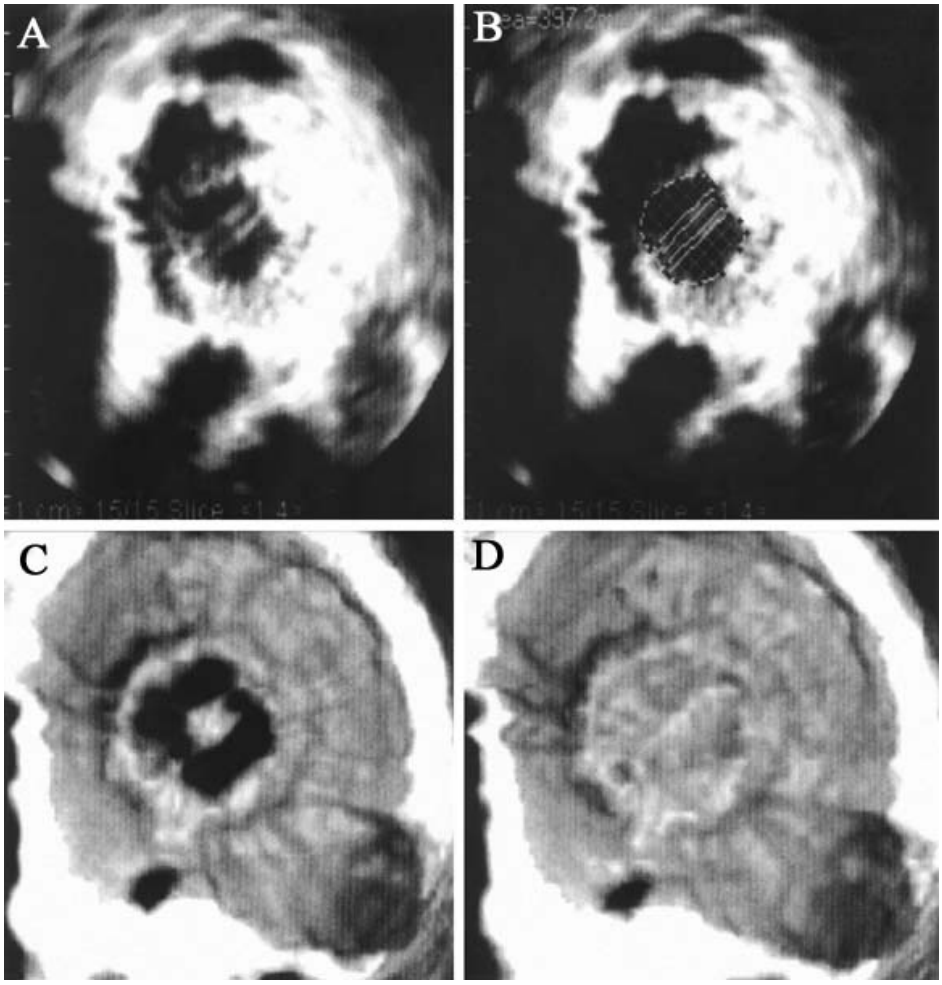

Figure 3 *Anyplane images at the short-axis level of a St Jude Medical valve prosthesis, in which the circumferences of the inner ring and both leaflets as well as the corresponding orifice area-3D measurement are shown (**A** and* B*). The corresponding surface-rendered images from the unroofed left atrium view looking down on the prosthesis in diastole and systole (**C** and **D**) are shown. Also note the enlarged left atrium and atrial appendage (at 5 o'clock). 3D, Three-dimensional.*

adjusted with the "slice mode" (paraplane echocardiography) in the short-axis tile. By slicing through the prosthetic valve ring from the superior to the inferior side, the segment in the most superior slice that showed a clear prosthetic inner ring and disk was measured at maximal valve opening. The inner contour of the prosthetic valve orifice was traced by using the area-measuring mode. Before measurement of the area, 2 perpendicular diameters of the prosthetic valve orifice in the short-axis cut plane were compared and verified with the diameters of the valve orifice in 2 perpendicular long-axis cut planes (Figures 1 and 2). The purpose of this measurement was to avoid errors in tracing caused by artifacts induced by the mechanical valve. The mean value of 3 consecutive measurements was calculated. In addition, the discharge coefficient was calculated from the orifice area (ie, orifice area-Doppler, orifice area-3D, or orifice area-literature divided by orifice area-manufacturer). In 14 patients, orifice area measurements

were repeated 1 month later in a blinded fashion for evaluation of the intraobserver and interobserver variabilities.

Table 1 Comparison of orifice areas (in cm^2) in patients after AVR and MVR

Group	N	OA-3D	OA-Doppler	OA-literature	OA-manufacturer
MVR	13	3.1 ± 0.6	2.7 ± 0.7	3.1 ± 0.1	4.3 ± 0.7*
AVR	11	2.2 ± 0.4	1.7 ± 1.0	1.5 ± 0.5	2.6 ± 0.8†
MVR + AVR	24	2.6 ± 0.7	2.3 ± 0.9	2.4 ± 0.9	3.6 ± 1.1*

AVR, Aortic valve replacement; MVR, mitral valve replacement; n, number of prosthetic valves studied; OA-3D, orifice area by 3-dimensional transesophageal echocardiography; OA-Doppler, orifice area by currently used Doppler methods for prosthetic assessment; OA-literature, orifice area by historical controls provided by Doppler literature; OA-manufacturer, orifice area by manufacturer's values.

**P < .01 for OA-manufacturer versus the other 3 groups.*

†P = .007 for OA-literature versus OA-manufacturer.

Volume- and surface-rendered display of the prosthetic valve prostheses

Volume and surface rendering is a 3D technique in which a depth perception is created and in which details of the surface in the region of interest can be shown. The volume- and surface-rendered view of the valve orifice can be derived directly from the short-axis cut plane. The optimal image is further adjusted by the resolution, threshold, and transparency settings according to the image quality (Figure 3).

Historical controls obtained from literature and manufacturer's values

Doppler-derived orifice areas from historical controls with normally functioning prostheses in the aortic and mitral valve positions for corresponding valve types and sizes were obtained from literature. For a prosthesis in the mitral valve position, pressure half-time derived values were taken as the reference values, and for a prosthesis in the aortic valve position, continuity equation-derived values were taken as the reference values.[8-13] The manufacturer's values were obtained from literature.[10,11,13]

Statistical analysis

Orifice areas by 3D TEE planimetry (orifice area-3D) were compared with Doppler data (orifice area-Doppler), with historical control values from literature (orifice area-literature), and with the geometric orifice areas provided by the manufacturers (orifice area-manufacturer). The data were expressed as mean ± 1 SD. One-way analysis of variance (Scheffé test, SPSS [Chicago, Ill] statistical software) and linear regression coefficients and equations were used to evaluate the results between orifice area-3D and orifice area-Doppler, orifice area-literature and orifice area-manufacturer, and also between the discharge coefficients. To compare the results of the intraobserver and

interobserver analyses, the coefficient of variation was calculated with the following formula:

$$\%\ \text{variability} = \frac{\sqrt{\sum_n \frac{(x_1 + x_2)^2}{n}}}{\sum_n \frac{1/2(x_1 + x_2)}{n}} 100\%$$

in which x1 = observer 1, x2 = observer 2, and n = number of observations.

A Bland-Altman plot was used to assess the difference between 2 methods (bias) and their limits of agreement (2 × SD). A paired t test was used for comparison of the prosthetic valve diameter as assessed by 3D TEE and of the diameters obtained from the manufacturer. A 2-tailed P value < .05 was considered statistically significant.

RESULTS

Two-dimensional transesophageal echocardiography and transthoracic Doppler

Normal disk opening and closure as well as transprosthetic gradients were observed by Doppler and 2D TEE; no abnormal regurgitation was found. The results for orifice area-3D, orifice area-Doppler, orifice area-literature, and orifice area-manufacturer are shown in Table 1 for the MVR group, the AVR group, and the total group (MVR + AVR). In the MVR + AVR and the MVR groups, orifice area-manufacturer was significantly larger than in the 3 other orifice areas. In the AVR group the difference was only significant between orifice area-manufacturer and orifice area-literature. The discharge coefficients for orifice area-Doppler, orifice area-3D, and orifice area-literature were 0.60 ± 0.18, 0.78 ± 0.16, and 0.67 ± 0.13, respectively. The 3D discharge coefficient was significantly larger (P = .002) than the Doppler coefficients.

Time required for 3-dimensional transesophageal echocardiography

Data acquisition for 3D TEE required 4 ± 2 minutes. Postprocessing of the raw data required 11 ± 3 minutes. Planimetric measurement took 30 ± 15 minutes once the operator was familiar with the system. Dynamic volume- and surface-rendered display took 3 ± 1 minutes.

Planimetric assessment of the valve area by 3-dimensional transesophageal echocardiography

Planimetric assessment of the mechanical prosthetic valve orifice area was possible in all 24 prostheses studied in 22 patients. The correlations and agreement between orifice area-manufacturer versus orifice area-3D and between the internal orifice diameter as provided by the manufacturer (diameter M) and the measured maximal internal diameter by 3D TEE (diameter 3D) are shown in Figure 4. For prosthetic valves in the aortic and mitral positions, regression equations and Bland-Altman analysis are shown separately in Figures 4 and 5. Bland-Altman analysis showed that the relative difference between diameter M and diameter 3D was small and insignificant for both prosthetic valves in the aortic and mitral positions: bias 0.14 cm and 0.14 cm; limits of agreement ±0.52 cm and ±0.34 cm; respectively (Figure 4). The bias and limits of agreement for orifice area-3D versus orifice area-manufacturer were larger: 0.49 ± 1.14 cm^2 for prostheses in aortic position and 1.27 ± 0.48 cm^2 for prostheses in the mitral position. In Figure 5, good-to-excellent correlations were observed for valve prostheses in the aortic position between orifice area-3D or orifice area-manufacturer versus orifice

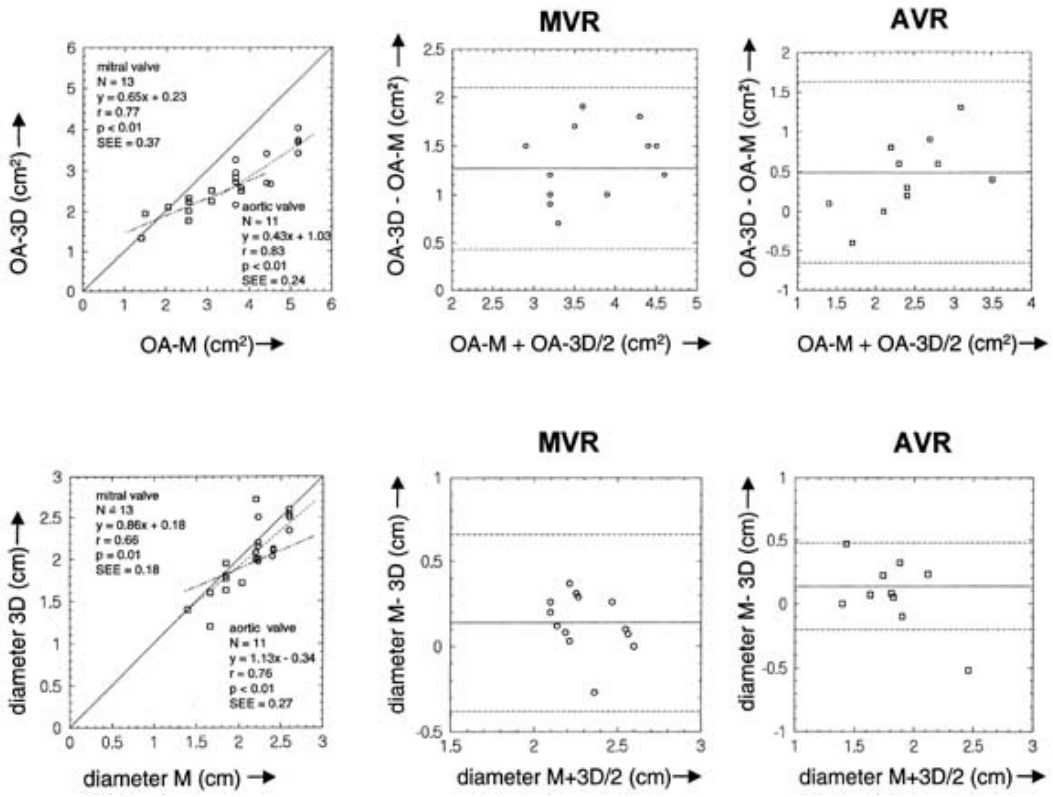

Figure 4 *The relation between orifice area-manufacturer (OA-M) and orifice area by 3-dimensional transesophageal echocardiography (OA-3D) shown as a linear regression plot (left upper panel). A similar plot is shown for the relation between the measured maximal internal diameter by 3-dimensional transesophageal echocardiography (diameter 3D) and the diameter as provided by the manufacturer (diameter M, left lower panel). The squares represent valve prostheses in the aortic position, and the dots represent valve prostheses in the mitral position. The number of cases studied (N), the linear regression coefficients (r), and their equations with the standard errors of the estimate (SEE) are shown, as well as the P values. The solid line represents the line of identity in the linear regression plots; the dashed lines are the regression lines for both types of valve prostheses. In the middle and right upper and lower panels, Bland-Altman plots are shown for prosthesis in mitral position (MVR) and aortic position (AVR) separately. In the Bland-Altman plot, the mean difference (bias) is represented by a solid line and the 95% confidence limits by both dashed lines.*

area-Doppler, and between orifice area-3D or orifice area-manufacturer versus orifice area-literature. For mechanical prosthetic valves in the mitral position, these correlations were poor to moderate.

Measurement variability

The coefficient of variation in the intraobserver analysis of orifice area-3D was 11% in the 14 patients studied again after 1 month. The interobserver variability was 21%.

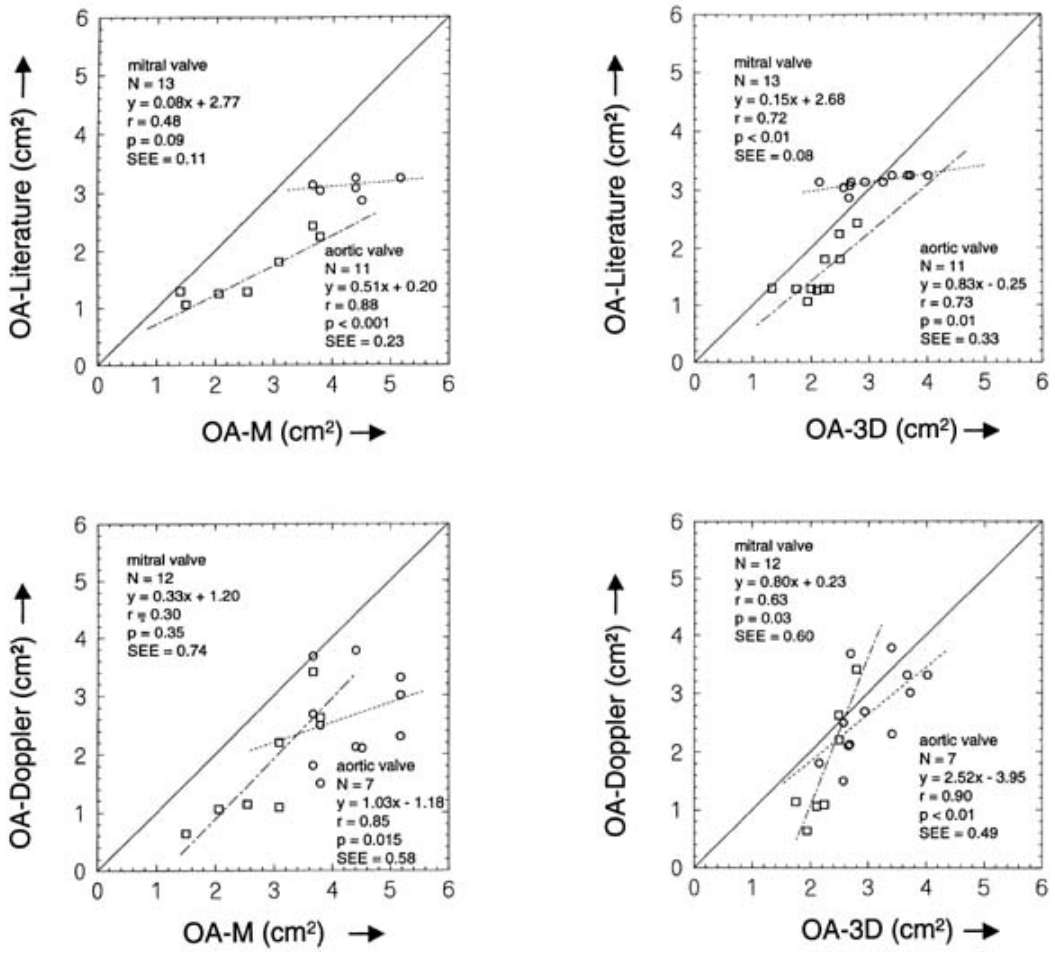

Figure 5 *Linear regression plots showing the relation between orifice area-manufacturer (OA-M) and orifice area-Doppler (OA-Doppler) and between OA-M and orifice area-literature (OA-literature) in the left panels. In the right panels, similar plots are shown for the relation between OA-3D versus OA-Doppler and OA-3D versus OA-literature. OA-3D, Orifice area by 3-dimensional transesophageal echocardiography; SEE, standard error of the estimate. (See Figure 4 for further description.)*

Volume- and surface-rendered display of valve prostheses

In 14 (58%) of 24 cases, high-quality images of the prosthetic valves could be reconstructed by volume and surface rendering. After rendering, valve dynamics could be displayed in cineloop format. In other cases, the volume- and surface-rendered images were of suboptimal quality because of artifacts originating from shadowing or because of multiple echoes reflected or acquired during the procedure.

DISCUSSION

Three-dimensional TEE has not been applied yet for accurate prosthetic valvular planimetry. Our report is the first to examine the feasibility of anyplane planimetric assessment of orifice area and compare it with Doppler data obtained during the same ultrasonographic examination, as well as with Doppler data from historical controls and with geometric orifice areas provided by the manufacturers. Orifice area assessment by 3D TEE is independent of flow, heart rate, systolic and diastolic left ventricular function, and mitral or aortic regurgitation, in contrast to orifice area-Doppler or orifice area assessment based on the Gorlin equation (including the pressure half-time method). The latter 2 methods have their own limitations and pitfalls and also underestimate orifice areas relative to the geometric orifice areas provided by the manufacturers.[2,14-18] The same is true for the orifice area assessment by the proximal isovelocity surface area method.[19] The laser flow imaging method and the 3D contrast imaging method of vena contracta areas seem promising, but they have been validated only in vitro so far.[20,21]

Orifice area assessment

In the present study, orifice area-3D correlates well with orifice area-manufacturer, with a better correlation than between orifice area-Doppler and orifice area-manufacturer. With respect to the correlation between Doppler-derived orifice areas and orifice area-manufacturer and orifice area-3D, the prostheses in the aortic position, in which the continuity equation was used, had a much better correlation than their counterparts in the mitral position, in which the pressure half-time method was used (Figure 5). This discrepancy in Doppler correlation between the pressure half-time method and the continuity equation method was even more pronounced in the orifice area-literature plots versus the orifice area-manufacturer and orifice area-3D plots, which is in keeping with previous reports.[8,9,19] This underscores the limitations of the pressure half-time method because this method also incorporates other factors such as atrioventricular compliance and pressure as well as ventricular relaxation. For prostheses in the aortic position, the underestimation of orifice area-Doppler relative to orifice area-manufacturer may have been caused by localized high-velocity jets in the St Jude valve prostheses (8 of 11 [73%] in this study). These jets affect the continuity equation calculation of orifice area-Doppler, resulting in a smaller calculated orifice area.[14]

Comparison with historical controls from Doppler literature showed similar results. There are 2 potential causes for underestimation of orifice area-3D relative to orifice area-manufacturer: ultrasound artifacts and pannus or thrombus ingrowth. Ultrasound artifacts (fuzzy contours and streaky patterns) are especially present on the disk(s) and to a lesser extent on the inner-ring boundary (Figures 1, 2, and 3). These artifacts on the disk(s) may occupy a large proportion of the inner-ring area, resulting in underestimation. They are probably the result of technical problems related to 3D TEE acquisition and processing (motion artifacts, ultrasound scattering, and reverberation). It is likely that the observed degree of underestimation for orifice area-3D (Figure 4) parallels the error in measurement of the projected area of the disk, which normally should be very small.[11] Therefore the bias and limits of agreement for valve prostheses in the aortic position were smaller (because their size was smaller) than those for prostheses in the mitral position.

The disks were included in the orifice area-3D measurement to allow a better comparison with orifice area-Doppler because flow resistance and thus, indirectly, the orifice area-Doppler of the valve are mainly determined by hydrodynamic factors acting

on the prosthetic disk. In mitral valve prostheses during acquisition for 3D TEE, the transducer is located just behind the left atrium near the valve orifice, which yields better image quality than the short-axis view of the mitral valve prosthesis obtained from the transgastric window. Aortic valve prostheses were technically more challenging, and images were generally less optimal in comparison with those of the mitral valve prostheses. This is probably the result of more shadowing artifacts caused by the relative orientation of the transducer and the prosthesis in the aortic position. In general, St Jude Medical valve prostheses in the mitral position were the easiest valve types to measure.

The 2D TEE criteria for thrombus[22] were absent in our patient population with normally functioning mechanical valve prostheses. A thin layer of pannus on the inner-ring surface, which does not yet interfere with normal opening and closure mechanics,[5] is unlikely to be detected as a cause of surface irregularities by the relatively limited resolution of the 3D technique.

Variability

Intraobserver variability for orifice area-3D assessment was low. However, interobserver variability was twice as high. The major part of the variability in the orifice area-3D measurement is likely the result of measurement error of the projected area of the disks, as already discussed. The positioning of the cut plane through the prosthesis was standardized, therefore this was not considered a major contributor to variability. If we consider the reported intraobserver and interobserver variabilities for orifice area-Doppler of 15% and 9%, respectively, for St Jude mechanical prostheses in the mitral position (pressure half-time method),[8] and 13% and 18%, respectively, for these prostheses in the aortic position (continuity equation),[9] these are reasonably comparable to the observed variability in the present study.

Limitations

Ball-in-cage-type valves (like the Starr-Edwards [Baxter Healthcare Corp, Edwards Division, Santa Ana, Calif] prosthesis) and bioprostheses were not examined. Furthermore, only patients with normal prosthetic function were examined, and the majority had normal left ventricular function. It is conceivable that poor left ventricular function may influence the opening angle of the leaflets, thereby affecting the measured orifice area-3D. In the patients with a (extremely) poor left ventricular function, however, the opening angle appeared to be maximal.

Clinical implications and conclusions

Orifice area by 3D TEE is feasible, provides direct measurement of orifice area of both prostheses in aortic and mitral positions, has a good correlation with orifice area-manufacturer and orifice area-Doppler, and has a larger discharge coefficient than the one obtained by Doppler. Orifice area assessment by 3D TEE, however, is more time consuming and requires more operator and analysis skill than conventional Doppler techniques. In our opinion, orifice area-3D is worth the effort because it is the only ultrasonographic technique that allows detailed morphologic in vivo assessment of mechanical valve prostheses, with more structural morphologic detail about the valve itself and its sewing ring, and allows functional assessment of valve kinetics, especially if the en face view with dynamic volume- and surface-rendered images is generated. It may be questioned whether orifice area-3D assessment is superior for pathologic conditions such as significant (prosthetic) regurgitation or low cardiac-output states, which clearly affect the Doppler-derived methods and the Gorlin method.[8,14] The orifice area-3D method may also provide better insight into the extent and mechanisms of valvular

obstruction and may be able to better differentiate pathologic obstruction from severe patient valve mismatch. It is conceivable that a complementary morphologic technique such as 3D TEE could be helpful in those cases in which Doppler analysis yields equivocal results. These issues need to be addressed in future studies.

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Chapter 5

ANTERIOR MITRAL VALVE ANEURYSM: EVALUATION BY THREE-DIMENSIONAL ECHOCARDIOGRAPHY

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ABSTRACT

Three-dimensional reconstruction of cardiac structures is becoming increasingly important. Complete spatial visualization of cardiac structures and their relation to each other enable better understanding of both morphologic and functional lesions. This report describes a patient with a mitral valve aneurysm, considered a rare pathologic condition in association with aortic valve endocarditis.[1-4]

CASE REPORT

A 46-year-old man was admitted to our hospital because of increasing dyspnea on effort. The patient had a history of endocarditis 2 years ago. On admission, physical examination revealed a 2/6 ejection systolic murmur at the aortic area and a 3/6 holodiastolic murmur at the left sternal border. There were no signs of peripheral edema or recurrent endocarditis.

Transthoracic echocardiography was of poor quality because of the nondiagnostic window, therefore transesophageal echocardiography was proposed. Multiplane transesophageal echocardiography revealed a prolapsing right coronary cusp of the aortic valve with echodense structures probably associated with previous endocarditis. In addition, a globe-shaped structure protruding toward the left atrium was visualized on the anterior mitral leaflet (Figure l, A). On Doppler color flow mapping, both aortic and mitral regurgitation were detected. The eccentric jet of aortic regurgitation was directed opposite to the anterior mitral leaflet (Figure 1, B). The color flow signal was visualized within the globe-shaped structure of the anterior mitral leaflet as well. The diagnosis of an anterior mitral valve aneurysm was suggested as a result of previous aortic valve endocarditis. Because it was reported that this lesion can be repaired surgically and because such an earlier decision might obviate the need for mitral valve replacement, we considered mitral valve reconstruction.[5] Unfortunately, the patient refused any surgical treatment.

During the multiplane transesophageal echocardiographic study, image acquisition for dynamic three-dimensional reconstruction was performed with a 5 MHZ, 64-element, multiplane transducer (Hewlett-Packard, Co., Andover, Mass.) connected to a Hewlett-Packard Sonos 2500 system. Cross-sectional cardiac images were obtained with a rotational probe carriage device from a fixed point in the esophagus at 3 degree increments starting from the horizontal plane. Each incremental step was controlled by a steering algorithm considering heart cycle variation and respiratory phase for optimal spatial and temporal registration. Transducer rotation over 180 degrees allowed us to fill conical data sets encompassing the region of interest. Cross sections were stored on an optical disk. Image processing and finally dynamic three-dimensional reconstruction by volume-rendering technique was performed off-line with the echo-scan system developed by Tom Tec GmbH (Munich, Germany).[6] To smooth the images while preserving sharp crossings, an anisotropic diffusion function was applied as well. This resulted in improvement of the image quality.

The reconstruction allowed a comprehensive morphologic analysis of the disease. The aneurysm of the anterior mitral valve was visualized in three-dimensional perspective in greater detail than by conventional imaging and helped to explain its formation. The “unroofed” view of the left atrium enables us to look at the aneurysm attached to the central part of the anterior mitral leaflet (Figure 2). The anterior mitral valve from within the left ventricle and a view into the left ventricular outflow tract in diastole visualize spatial relations of these structures (Figure 3).

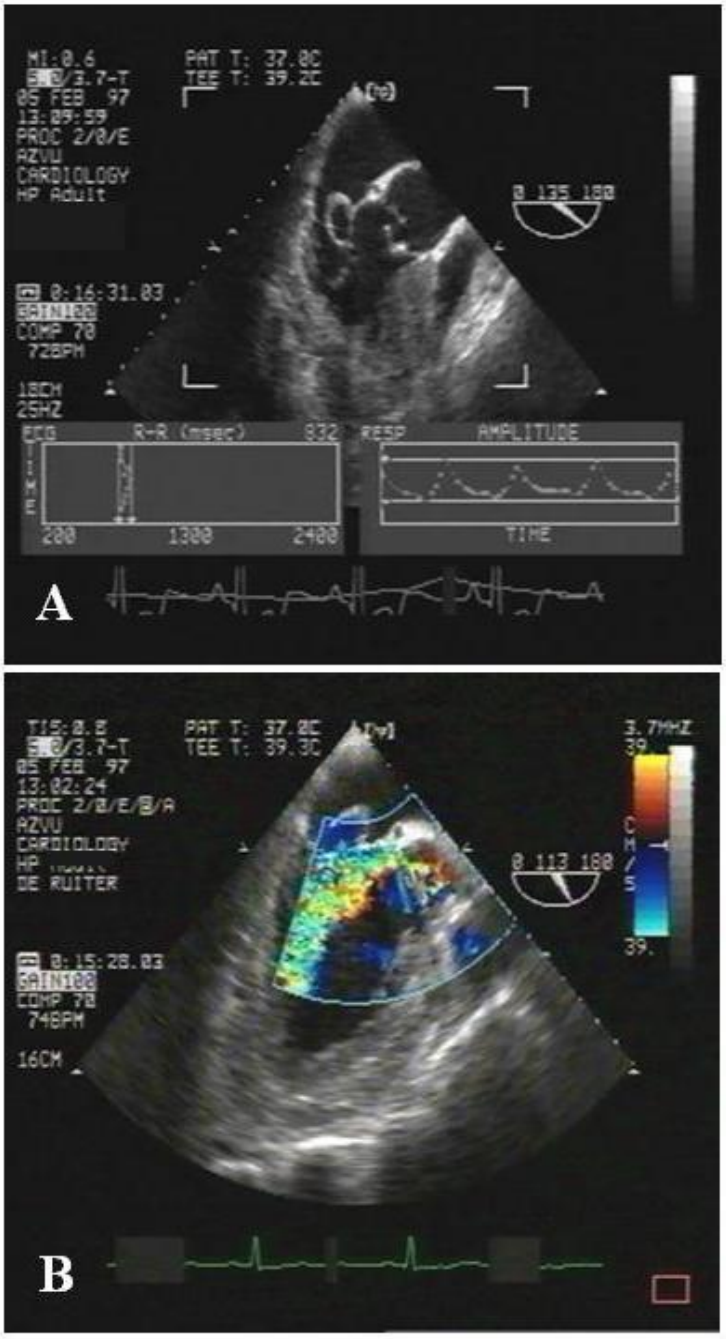

Figure 1 *Multiplane transesophageal echocardiographic views.* ***A****, Aneurysm located on the anterior mitral leaflet and prolapsed aortic valve.* ***B****, Color Doppler imaging reveals the regurgitant jet originating from the prolapsed aortic valve. Note the direction of the jet toward the anterior mitral leaflet.*

DISCUSSION

Three-dimensional reconstruction facilitates the study of structures of complex morphology. Therefore, details of cardiac anatomy can be readily appreciated. Our case demonstrates the probable mechanism of the anterior mitral valve aneurysm formation.

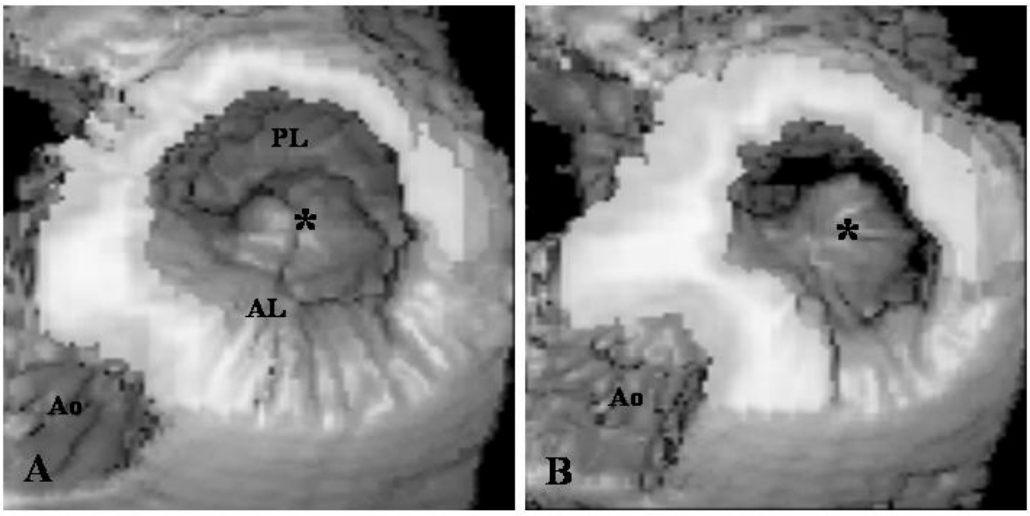

Figure 2 *Three-dimensional reconstruction of the mitral valve aneurysm.* ***A****, "Unroofed" view of the left atrium showing a globe-shaped structure (*) on the anterior mitral leaflet (AL) protruding into the left atrium in systole.* ***B****, Same valve in diastole. Ao, Aorta; PL, posterior mitral leaflet.*

Aneurysm of the mitral valve is considered to be an abnormality most commonly associated with aortic valve endocarditis. It can be speculated that the eccentric regurgitant jet emerging from the prolapsing aortic valve gives rise to aneurysm formation of the anterior mitral leaflet. This continuous turbulent flow leads to endocardial damage of the mitral valve and eventually may cause its perforation.[4] In addition, the right coronary cusp of the aortic valve when it prolapses is responsible for the development of such a unique entity. As regards spatial relations of these structures seen on three-dimensional images, the mechanism of aneurysm formation is obvious. If the patient had undergone the operation, the surgeon would have had a preview before the procedure; it would have been of value in guiding the mitral valve reconstruction.

Three-dimensional echocardiography is a new and evolving cardiac imaging technique. At present, the procedure is time consuming, requiring approximately 1 hour to process the images. Although on-line reconstruction is not feasible, some currently available echocardiographic machines with the rotational multiplane transducer allow acquisition of the two-dimensional data during routine transesophageal echocardiography, and if necessary, three-dimensional reconstruction can be performed afterward. Poor resolution of thin structures (for example, chordae), increasing amounts of nonstructural echoes, and dropout in valves imitating holes (for example, aortic or mitral valves) are limitations of three-dimensional echocardiography. Despite these limitations, we believe that three-dimensional echocardiography will soon find clinical application in greater dimension and enhance our ability to diagnose and treat cardiac disease. However, the complexity of image registration and reconstruction at the present time do not currently favor three-dimensional echocardiography over conventional two-dimensional echocardiography for the anatomic delineation of this type of aneurysm.

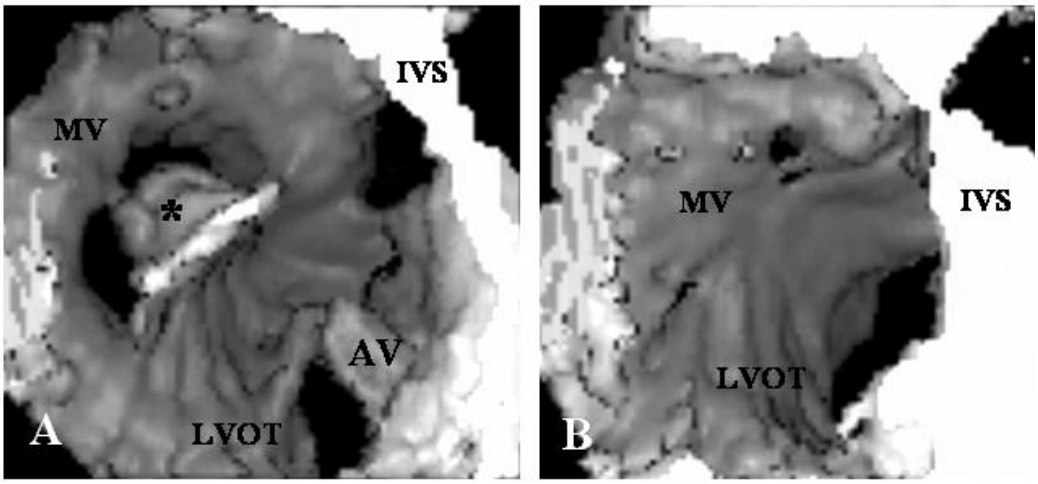

Figure 3 *Short-axis section of a three-dimensional reconstruction of the heart.* ***A****, Mitral valve (MV) is seen within the left ventricle in an open position in diastole. In addition, the left ventricular outflow tract (LVOT) is visualized with the prolapsing right coronary cusp of the aortic valve (AV) opposite to the aneurysm (*).* ***B****, Same view in systole. IVS, Interventricular septum.*

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Chapter 6

ASSESSMENT OF THE LEFT ATRIAL APPENDAGE MECHANICAL FUNCTION BY THREE-DIMENSIONAL ECHOCARDIOGRAPHY

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ABSTRACT

Aims. We evaluated the feasibility of three-dimensional echocardiography (3DE) in the assessment of left atrial appendage (LAA) function.

Methods and results. Forty-five patients underwent multiplane transesophageal echocardiography (TEE). In addition to Doppler and two-dimensional echocardiography (2DE), data for 3DE reconstruction were obtained during TEE. LAA ejection fraction based on 3DE volume measurements (EFv) and 2DE area measurements (EFa), coupled with other echocardiographic data, were related to LAA late peak emptying velocity (PEV), a frequently used indicator of LAA function. Multiple regression analysis has revealed a significant association of PEV with EFv ($p<0.0001$), spontaneous echocardiographic contrast ($p=0.001$), tricuspid regurgitation ($p=0.03$) and left ventricular hypertrophy ($p=0.05$). No significant relation was observed between PEV and EFa, presence or absence of atrial fibrillation, left ventricular dysfunction, mitral stenosis and insufficiency, left atrial dilatation, pulmonary venous peak systolic, diastolic and peak reverse flow velocity at atrial contraction as well as LAA volumes derived from 2DE and 3DE. In a simple linear correlation, the degree of association between PEV and EFv was higher as between PEV and EFa ($r=0.7$ versus 0.4, both $p<0.001$). Observer variabilities for calculating EFv were considerably lower than for 2DE derived EFa. Ejection fractions determined by 2DE area measurements at 45°, 90° and 135° cutplane angulations were related to EFv only at 135.°

Conclusions. LAA ejection fraction calculation by 3DE is feasible, more accurate than by 2DE and has lower observer variability. Furthermore, an optimal cutplane angulation of the LAA view at 135° has been demonstrated.

Key words: Left atrial appendage, transesophageal echocardiography, three-dimensional echocardiography, atrial fibrillation.

INTRODUCTION

The left atrial appendage (LAA) has an important role in cardiovascular performance[1]. Furthermore, its dysfunction is related to thromboembolic complications.[2-5] Thanks to transesophageal echocardiography (TEE), it is possible to visualize the LAA and assess its function by means of Doppler flow velocity interrogation and even ejection fraction calculation.[6,7]

The LAA is a structure that varies in volume and shape.[8,9] This variability should be considered in particular when two-dimensional echocardiography (2DE) is used for LAA ejection fraction calculation. Recently introduced three-dimensional echocardiography (3DE) allows measurements without geometric assumption.[10,11] It provides more accurate data than 2DE, as far as the structures with complex three-dimensional anatomy are concerned. Therefore, it should be an ideal tool for studying the LAA function by means of volume and ejection fraction measurements. Besides Doppler evaluation of the LAA function, it can be important just as left ventricular volume and ejection fraction calculations. To our knowledge, no data so far are available with respect to functional assessment of the left atrial appendage by 3DE. Thus, the aims of this study were: 1) to evaluate feasibility of 3DE for LAA volume and ejection fraction calculation. This was done by analysing the relation of LAA volumes and ejection fraction assessed by 2DE and 3DE as well as other echocardiographic data to the LAA late diastolic peak emptying velocity (PEV). The variability of LAA ejection fraction from two-dimensional area measurements and three-dimensional volume measurements was compared using intra- and interobserver studies. Furthermore, 2) the effect of cutplane angulation on LAA area measurements was studied in order to define the optimal 2DE tomographic imaging plane of the LAA.

METHODS

Patients

The study population included 45 patients with an indication for TEE (20 men and 25 women) and ranged in age from 26 to 84 years (mean age 59.5 $\pm$ 14.4 years). Of these 45 patients, 17 had combined mitral valve stenosis and insufficiency, 22 pure mitral valve insufficiency, 3 patients had pure mitral stenosis and 3 were without mitral valve involvement. Twenty-nine (64%) patients were in sinus rhythm and 16 (36%) in atrial fibrillation during the TEE examination. Characteristics of the patients are shown in Table 1. The study patients were originally examined for mitral valve disease, i.e. mitral stenosis, mitral insufficiency or a combination of both. Because during acquisition of data for 3DE reconstruction also the LAA was included, this study population was suitable for 3DE evaluation of the LAA.

Echocardiography

All enrolled patients underwent multiplane TEE examination, including a study of LAA function. Examinations were performed with a multiplane 5 MHz, 64-element transducer (Hewlett-Packard Co., Andover, Mass.) connected to a Hewlett-Packard Sonos 2500 or 5500 (Hewlett-Packard Co., Andover, Mass.). After the diagnostic multiplane transesophageal study, the probe was located at midesophageal level. A test sequence with 180 degrees rotation of the transducer array was performed to ensure whether the LAA was encompassed within the conical data set. The acquisition was performed at 3-degree increments with electrocardiographic (ECG) and respiratory gating. The data were stored on a magneto-optical disk and processed off-line using a 3DE system (Echo-Scan 3.1,

TomTec GmbH, Munich, Germany). 2DE and Doppler studies were recorded on VHS videotape.

Table 1 Clinical and Echocardiographic Variables

Age (yrs)	59.5 ± 14.4
Men/women	20/25
Sinus rhythm/atrial fibrillation	29/16
LAA peak emptying velocity (cm/s)	35.6 ± 21.7
LAA end-diastolic area (cm^2)	6.5 ± 2.9
LAA end-systolic area (cm^2)	4.4 ± 2.7
LAA end-diastlic volume (ml)	13.8 ± 8
LAA end-systolic volume (ml)	9.9 ± 7.3
EFa (%)	35.3 ± 17.2
EFv (%)	34.4 ± 15.4
Pulmonary peak systolic flow velocity (cm/s)	36.8 ± 23.3
Pulmonary peak diastolic flow velocity (cm/s)	38.8 ± 21.5
Pulmonary reversal flow at atrial contraction (cm/s)	13.7 ± 12.4
Left ventricular dysfunction (n=10)	
mild	6
moderate	4
severe	0
Mitral regurgitation (n=39)	
1+	23
2+	7
3+	9
Mitral stenosis (n=20)	
area (cm^2)	1.53±0.77
Tricuspid regurgitation (n=32)	
1+	23
2+	7
3+	2
Left atrial spontaneous echocontrast	15
Left atrial dimension	44.9±7.8
Left ventricular hypertrophy	3

LAA and pulmonary venous flow were evaluated by pulsed-wave Doppler interrogation. The PEV, as an indicator of LAA mechanical function, was obtained in the LAA long-axis view with the sample volume placed 1 or 2 cm within the appendage outlet. The values of three and five measurements were averaged in patients with sinus rhythm and atrial fibrillation, respectively. In addition, the presence of spontaneous echocardiographic contrast was determined in the LAA. Mitral and tricuspid insufficiency was graded semiquantitatively according to the maximum regurgitant jet area as assessed by color Doppler flow imaging. Left ventricular dysfunction was assessed by visual estimation and graded as mild, moderate and severe.

LAA volumes and ejection fraction were calculated from the 3DE volumetric data set by using Simpson's rule. After the long-axis view of the LAA had been selected, end-diastolic (EDV) and end-systolic volumes (ESV) were calculated by manual tracing of sequential short-axis views. In patients who were in sinus rhythm, LAA diastole was measured at the onset of the ECG P-wave and LAA systole at the ECG R-wave. Minimal and maximal areas were selected as end-diastole and end-systole in patients in atrial fibrillation. A line drawn from the limbus of the confluence of the left upper pulmonary vein and the LAA to the outermost portion of the mitral annulus was considered as a boundary between the cavity of the left atrium and the LAA. The paraplane technique was used to generate a series of equidistant cross-sections at fixed 3 mm slice thickness. When manual tracing was completed, the volume of the short-axis slice was calculated. Adding up the volumes of all slices provided the volume measurement (Figure 1). The percent volume ejection fraction of the LAA (EFv) was calculated as (EDV - ESV) / EDV. The same 3DE data set was used to generate a two-dimensional long-axis view of the LAA. End-diastolic area (EDA) and end-systolic area (ESA) was planimetred and percent area ejection fraction (EFa) was calculated (Figure 2). Intra- and interobserver reproducibility of all measurements was obtained in every patient by one observer at least two weeks apart and by two observers in a blinded fashion. In order to evaluate the errors caused by suboptimal cutplane selection, the LAA area and EFa was also measured in long-axis views angulated by 45°, 90° and 135° from the initially selected long-axis view. However, the cutplane angulations were not determined from the original 2DE images but within a 3DE data set, these views can be similar to real cutplanes during the multiplane TEE, because a 0° angulation is identical to a 0° imaging plane of multiplane TEE.

Statistical analysis

Data are reported as mean + SD. The effect of several independent variables (those obtained during the diagnostic TEE study and 3DE) upon PEV was studied using multiple linear regression analysis. The subset of predictor variables which gives the best fitting model was calculated. Correlations were studied using the Pearson correlation test. A p-value <0.05 was considered significant. Observer variability was assessed by coefficient of variation (calculated as standard deviation of the differences between measurements divided by the average value). Furthermore, the correlation coefficient (r), the mean difference and standard deviation were used for the intra- and interobserver study.

RESULTS

3DE reconstruction and volume calculation was feasible in all patients. The mean $\pm$ SD of the LAA EDV and ESV and ejection fraction obtained by 3DE were: 13.8 $\pm$ 8 ml, 9.9 $\pm$ 7.3 ml and 34.4 $\pm$ 15.4 %, respectively. The mean values $\pm$ SD of the LAA EDA and ESA and ejection fraction measurement using 2DE were: 6.5 $\pm$ 2.9 cm^2, 4.4 $\pm$ 2.7 cm^2 and 35.3 $\pm$ 17.2 %, respectively. In multiple linear regression analysis, PEV was significantly

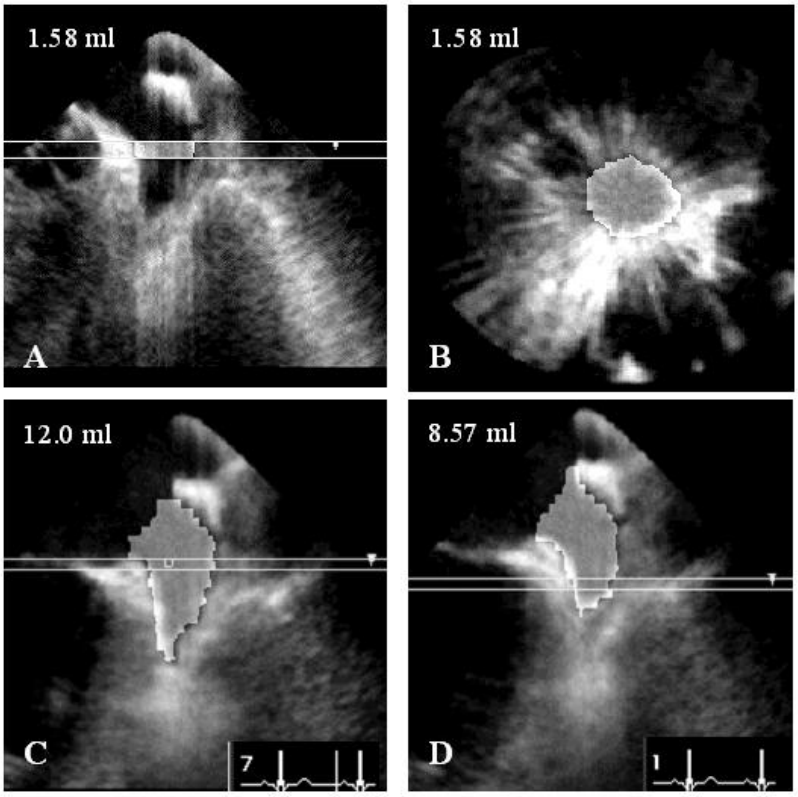

Figure 1 *(A) LAA volume measurement by 3DE using Simpson's rule. A slice of 3 mm thickness is measured in the long-axis plane of the LAA. (B) Contour tracing and labeling of the slice in the short axis. After tracing and labeling, the volume of the entire LAA is displayed in the reference image and the end-diastolic (C) and end-systolic (D) volume is calculated.*

related to 3DE derived LAA ejection fraction (EFv, $p<0.0001$), spontaneous echocardiographic contrast ($p=0.001$), tricuspid insufficiency ($p=0.03$) and left ventricular hypertrophy ($p=0.05$). There was no significant relation of PEV to other observed variables: presence or absence of atrial fibrillation ($p=0.4$), left ventricular function ($p=0.07$), mitral stenosis ($p=0.3$), mitral insufficiency ($p=0.09$), ESV ($p=0.2$), EDV ($p=0.3$), ESA ($p=0.2$), EDA ($p=0.3$), EFa ($p=0.1$), left atrial dilatation ($p=0.06$), pulmonary venous peak systolic, diastolic and peak reverse flow velocity at atrial contraction ($p=0.2$, $p=0.6$, $p=0.5$, respectively). Following a best subset selection a final regression model was: PEV = 30.87 -5.64 tricuspid insufficiency + 63.97 EFv - 7.29 left atrial dilatation - 16.1 left atrial spontaneous echocardiographic contrast - 17.19 left ventricular hypertrophy. In a simple linear correlation, the degree of association between PEV and EFv was higher as between PEV and EFa ($r=0.7$ vs $r=0.4$, both $p<0.001$, Figure 3). Observer variabilities are presented in Table 2. There were considerably closer limits of agreement, lower variability and higher correlation in ejection fraction calculation by 3DE as compared with 2DE. Ejection fractions determined by 2DE area measurements at 45°, 90° and 135° cutplane angulation (mean $\pm$ SD: 34.1 $\pm$ 18.5 %, 34.0 $\pm$ 19.2 %, 34.3 $\pm$ 17.9 %) were not significantly different (in multiple comparison each p-value not significant). However, by multiple regression analysis a significant relation was found between EFv and EFa

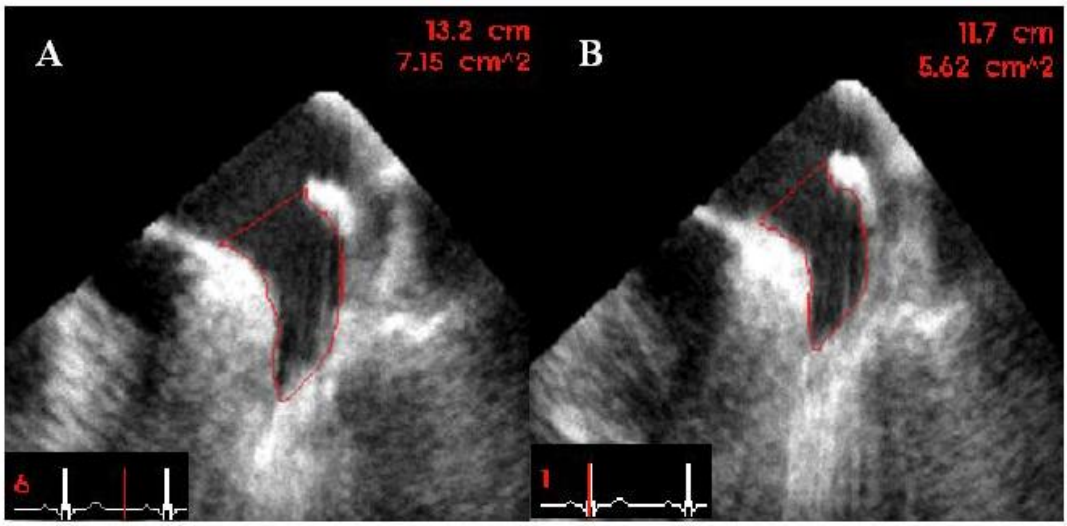

Figure 2 *The principle of left atrial appendage ejection fraction measurement using two-dimensional area method. From the three-dimensional data set an end-diastolic (A) and end-systolic (B) long-axis view is used for percent area ejection fraction calculation.*

measured at 135° cutplane angulation (p=0.008) but not at 45°and 90° angulation (p=0.3 and 0.8).

DISCUSSION

Besides Doppler evaluation of the LAA, numerous studies have reported assessment of the LAA function by area and ejection fraction calculation. These studies led to recognition that the percent area ejection fraction of the LAA can be related to successful restoration of the sinus rhythm from atrial fibrillation.[12] LAA dysfunction, using area ejection fraction calculations, was also demonstrated in patients with dilated and hypertrophic cardiomyopathy.[13] Similarly, these measurements based on 2DE were used for presentation of more depressed LAA function in patients in atrial flutter with intermittent atrial fibrillation as compared to pure atrial flutter.[14] Improvement of the LAA ejection fraction after treatment of heart failure also revealed its relation to the overall cardiac performance.[15] In the study by Porte et al.,[16] some discrepancy has been encountered in the assessment of LAA function after successful percutaneous mitral commissurotomy: PEV was positively associated with successful commissurotomy as well as LAA ejection fraction derived from the transverse plane but not from the longitudinal plane. This was related to the difficulties inherent in the planimetry method carried out on two-dimensional images and rotational movements of the heart. In some reproducibility studies, percent area ejection fraction measurement is prone to observer variability, primarily because of complex three-dimensional anatomy of the LAA, which limits accurate definition of the standard tomographic imaging plane.[4,15] In our study, the correlation between EFa and PEV was lower than the correlation between EFv and PEV. In addition, there was higher reproducibility in EFv calculation than EFa in both the intra- and interobserver studies. Besides the PEV-EFv association, we found other echocardiographic correlations such as left atrial spontaneous echocardiographic contrast,

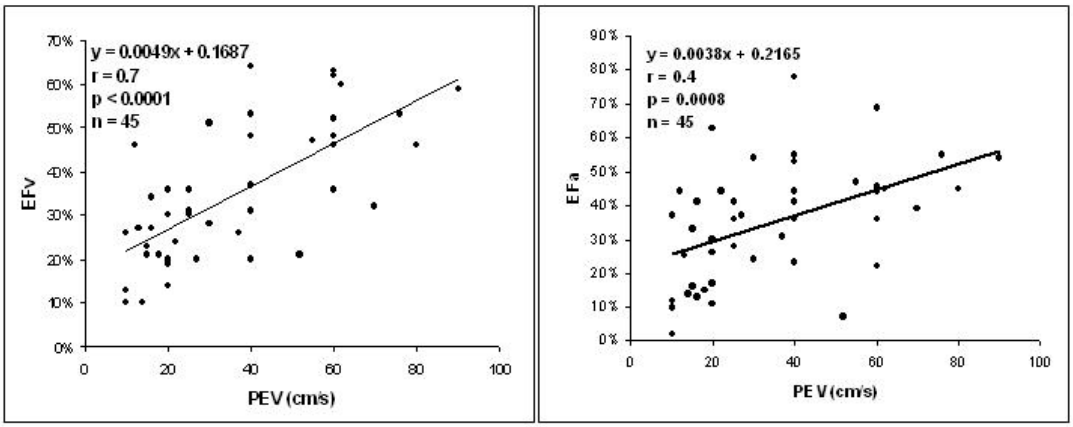

Figure 3 *Scatterplot of linear regression analysis of the left atrial appendage (LAA) volume ejection fraction (EFv) and area ejection fraction (EFa) versus LAA late diastolic peak emptying velocity (PEV).*

tricuspid insufficiency and left ventricular hypertrophy. A negative correlation between PEV and spontaneous echo contrast indicates a well known relation of LAA dysfunction to thrombus formation.[17-20] Influence of tricuspid insufficiency on LAA PEV suggests that increased left atrial pressure transmitted to right heart chambers is inversely related to LAA function.[21] Association of PEV and left ventricular hypertrophy in our study is consistent with the results of the Stroke Prevention in Atrial Fibrillation (SPAF-III) study, which confirmed that a history of hypertension was more frequently associated with LAA thrombi and cardioembolic stroke.[22,23]

The above mentioned points to the probably higher accuracy of 3DE in LAA ejection fraction calculation compared to 2DE. As opposed to 2DE, 3DE provides a homogeneous data set in which volume measurements are independent on the irregularities of the LAA and movements of the heart. The echocardiographic data in this study were related to the LAA late peak emptying velocity. This is an accepted functional index of the LAA and in vivo there is no other method to test the feasibility of 3DE measurements.

The optimal tomographic imaging plane of the LAA has not been sufficiently defined. Therefore, we assessed the effect of cutplane angulation on the relation between EFa and EFv. Area ejection fraction at 135° angulation was only associated with EFv. This might be taken into account when multiplane TEE is used for LAA area measurements. Our observation is in agreement with the results found by Chan et al.,[24] who demonstrated greater LAA neck width and cross-sectional area at 135° than at 45° or 90.°

The present study has some important limitations: 3DE is still time-consuming, however, future development of faster computers, application of automatic border detection and on-line acquisition by real-time 3DE will shorten the time needed for three-dimensional reconstruction. Although one could argue that PEV can be measured much easier than volume and ejection fraction, Doppler flow measurement does not reflect the degree of LAA enlargement. This can be important because severely hypokinetic and dilated LAA predisposes to thrombus formation such as left ventricular aneurysm predisposes to thrombus formation. Therefore, we suppose that LAA volume and ejection

fraction calculations can be important just as left ventricular volume and ejection fraction measurements.

Table 2 Observer variabilities

	Mean difference ± SD		Intraobserver variability (%)	Interobserver variability (%)
	Intraobserver study	**Interobserver study**		
EFv	0.0002 ± 0.03	0.02 ± 0.08	8.8	22.8
EFa	0.0006 ± 0.15	0.03 ± 0.21	44.10	60
	C-SEE (%)		**Correlation coefficient**	
	Intraobserver study	**Interobserver study**	**Intraobserver study**	**Interobserver study**
EFv	8.8	22.8	0.97	0.89
EFa	40	58.8	0.61	0.34

Well established conditions (i.e. LV function, mitral stenosis and atrial fibrillation) which would have affected PEV, showed no significant relation in this study. The explanation can be that only 4 patients with severely impaired and 6 patients with moderately impaired LV function were present in this study. Regarding mitral stenosis, only 3 patients with pure mitral stenosis were included, remaining 17 patients had combined mitral stenosis and insufficiency. It is likely that this heterogeneous group of patients with mitral valve disease failed to show a hemodynamic effect of mitral stenosis on LAA function. A lack of correlation between PEV and atrial fibrillation may result from a wide continuum of LAA contractile dysfunction in patients with atrial fibrillation, from relatively preserved contraction to complete paralysis of the appendage. Despite the above mentioned, to our knowledge, this is the first study which has proved the feasibility of 3DE in the assessment of LAA mechanical function.

In conclusion, 3DE in the assessment of LAA ejection fraction is feasible and has lower observer variability compared to 2DE. It may complement 2DE and Doppler echocardiography in the assessment of LAA mechanical function. Future developments will simplify the procedure and expand its clinical applicability.

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Chapter 7

SUMMARY

The studies presented in this thesis assessed the feasibility and accuracy of quantitative three-dimensional (3D) echocardiography in the evaluation of mitral valve disease using conventional 3D measurements as well as new indices. We studied the additional value of 3D transesophageal echocardiography for patients with mitral valve stenosis undergoing percutaneous mitral balloon valvotomy. Furthermore, we studied the feasibility of prosthetic orifice area measurement by 3D anyplane transesophageal echocardiography in patients with normally functioning valve prostheses in the mitral and aortic positions. Finally, the left atrial appendage mechanical function was assessed by 3D echocardiography.

We demonstrated that:

§ 3D echocardiography allows reproducible measurement of mitral valve stenosis. The presented study confirmed the moderate correlation between mitral valve area assessed by anyplane echocardiography and 3D surface rendering when compared to Doppler PHT-derived areas. We have described a new index, the doming volume, which allows quantification of the mobility and 3D geometry of the mitral valve. Patients with a flat geometry of the mitral valve have a propensity to atrial fibrillation. Mitral valve volume can be used for quantitative evaluation of mitral stenosis and tends to be greater in patients with critical stenosis.

§ 3D transesophageal echocardiography provides additional information to two-dimensional (2D) echocardiography in patients with mitral valve stenosis undergoing percutaneous mitral balloon valvotomy. It can be a valuable alternative when assessment of the mitral valve area by 2D transthoracic echocardiography is not reliable. The mitral valve volume can be assessed by 3D transesophageal echocardiography. Mitral valve volume is inversely correlated to a successful valvuloplasty procedure and can possibly be useful for the selection of patients for mitral balloon valvotomy. Post-balloon valvotomy 3D transesophageal echocardiography improves the description of the valvular anatomy. This enables more understanding of the mechanisms of successful mitral balloon valvotomy and its complications.

§ 3D transesophageal echocardiography provides direct measurement of orifice area of both prostheses in aortic and mitral positions, has a good correlation with orifice area-manufacturer and orifice area-Doppler, and has a larger discharge coefficient than the one obtained by Doppler techniques. However, it is time consuming, 3D echocardiography allows detailed in vivo assessment of mechanical valve prostheses, with more structural morphologic detail about the valve itself and its sewing ring, and allows functional assessment of valve kinetics, especially if the en face view with dynamic volume- and surface-rendered images are generated.

§ We demonstrated that 3D echocardiography is feasible in the assessment of the left atrial appendage ejection fraction and has lower observer variability compared to 2D echocardiography. So, it may complement 2D and Doppler echocardiography in the assessment of the left atrial appendage mechanical function. Furthermore, an optimal cutplane angulation of the left atrial appendage view at 135° has been demonstrated.

§ The assessment of the morphology, function and pathology of the heart, and especially the mitral valve apparatus by 3D echocardiography becomes more accurate. Comparing with 2D echocardiography, 3D echocardiography offers advantages for the morphologic and quantitative assessment of mitral valve. 3D echocardiography provides new quantative indices unobtainable by conventional 2D imaging. It appears that 3D echocardiography has the potential for planning operations and assessing interventional or surgical results.

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